

Prostate cancer imaging

Imaging in the Diagnosis and Management of Prostate Cancer

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Disclosures

- Inventor of US-Government owned patents:
 - A method of MRI-TRUS Fusion biopsy
 - A method of computer aided diagnosis (CAD) of prostate cancer
 - Another method of CAD for prostate cancer
 - A method of photoimmunotherapy
- CRADAs with GE, Philips, Philips-In vivo, Rakuten Medical-Aspyrian
- No financial disclosures to report

Diagnosing prostate cancer.

Men >50 years of age get routine screening prostate specific antigen (PSA) blood test

If they see a urologist they may get a digital rectal exam

If either are abnormal they undergo a transrectal prostate biopsy

Ultrasound guided biopsy

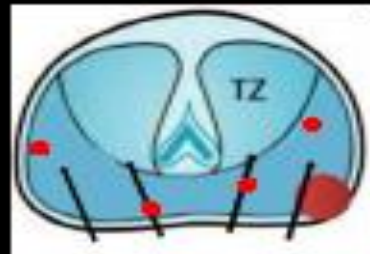
Problems with the Transrectal Ultrasound Guided Biopsy

Underdiagnosis



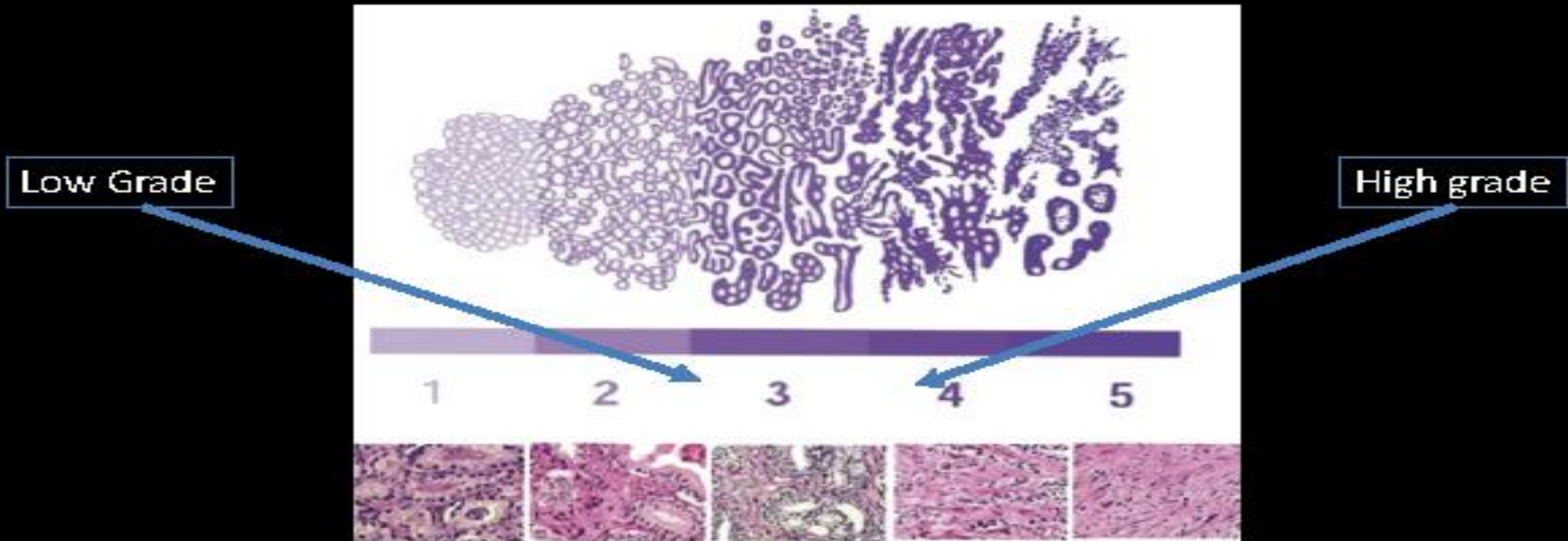
Poor Sampling

Overdiagnosis



Spectrum of diseases

Prostate Cancer is a Spectrum of Diseases



Prostrate cancer treatment

For men with low grade cancers: Active Surveillance

For men with intermediate-high grade: Radiation Therapy or Surgery

PSA tests are obtained to monitor for recurrence

**~30% of men will show rising PSA indicating possible recurrence
Known as “biochemical recurrence”**

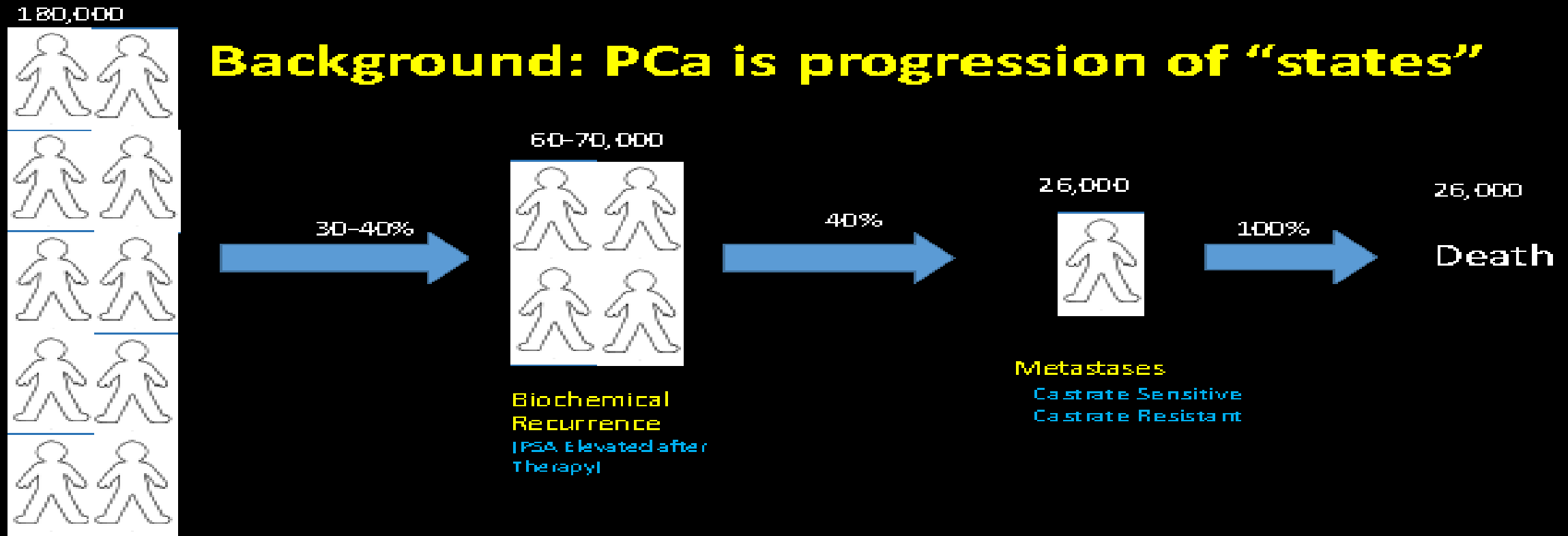
Prostate Cancer can spread to nodes and bones: metastatic prostate cancer

Treated with androgen deprivation therapy (ADT): met Castrate sensitive PCA

When ADT fails: metastatic Castrate resistant PCA

Pca progression

Background: PCa is progression of “states”

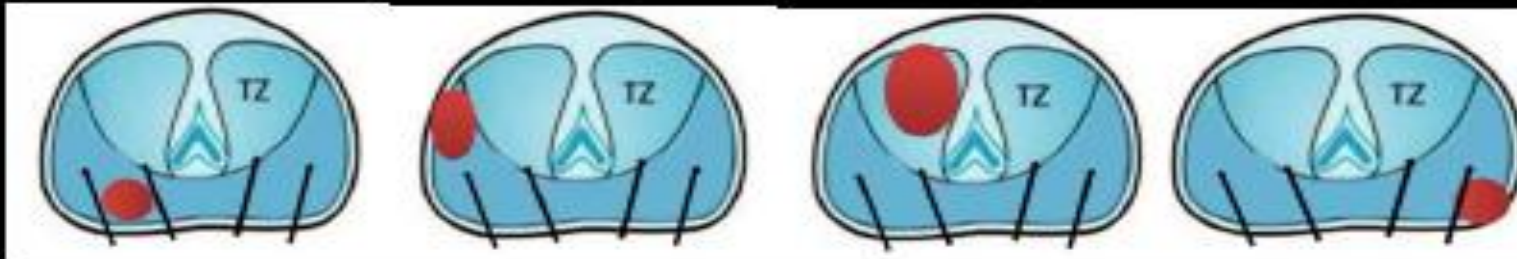


Primary Treatment

Ken Pienta, PCF 2017
Howard Scher JCO 2005

Diagnosis

Diagnosis



"Why is the prostate the only organ in the body that is biopsied blind?" Peter Pinto, MD circa 2003

Multi-parametric MRI

Multi-parametric Prostate MRI



3 Tesla MRI

T2 Weighted MRI
Diffusion Weighted MRI (DWI)
Dynamic Contrast Enhanced MRI (DCE)



Endorectal coil



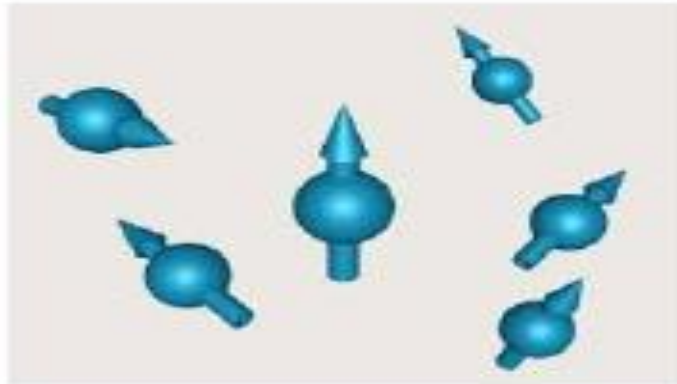
16-channel
cardiac coil



Baris Turkbey, MD

MRI physics

MRI Physics 101



Protons in space: no field

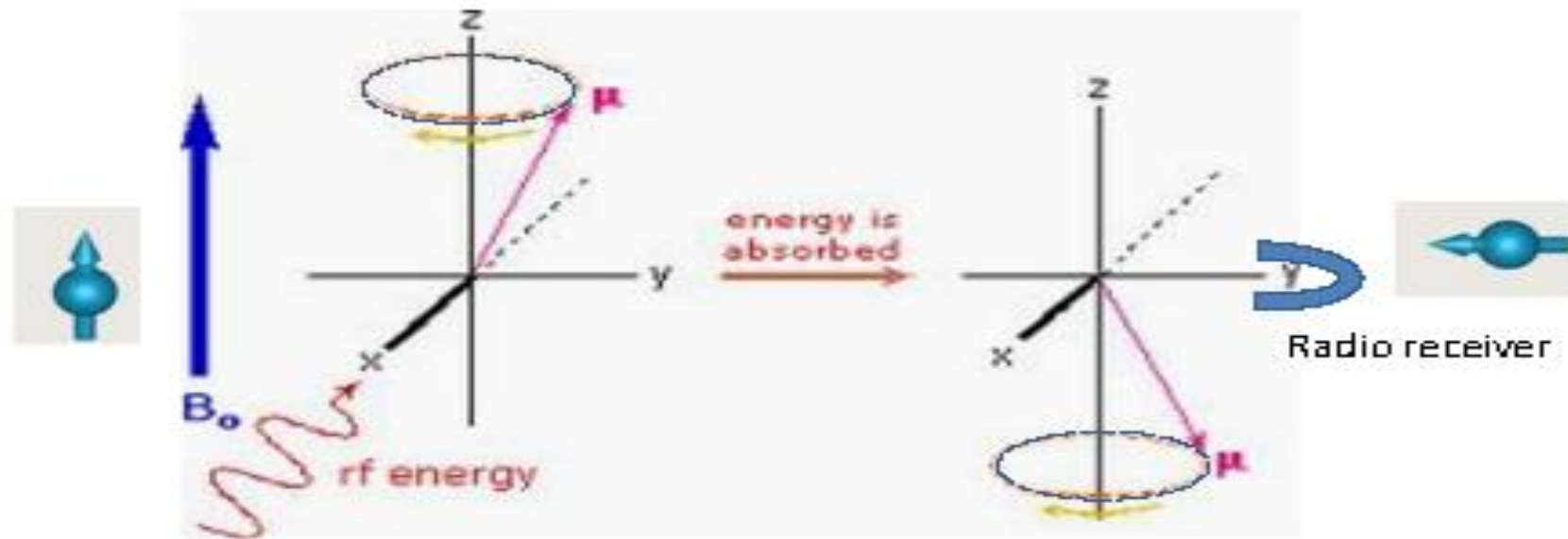


Protons in magnetic field



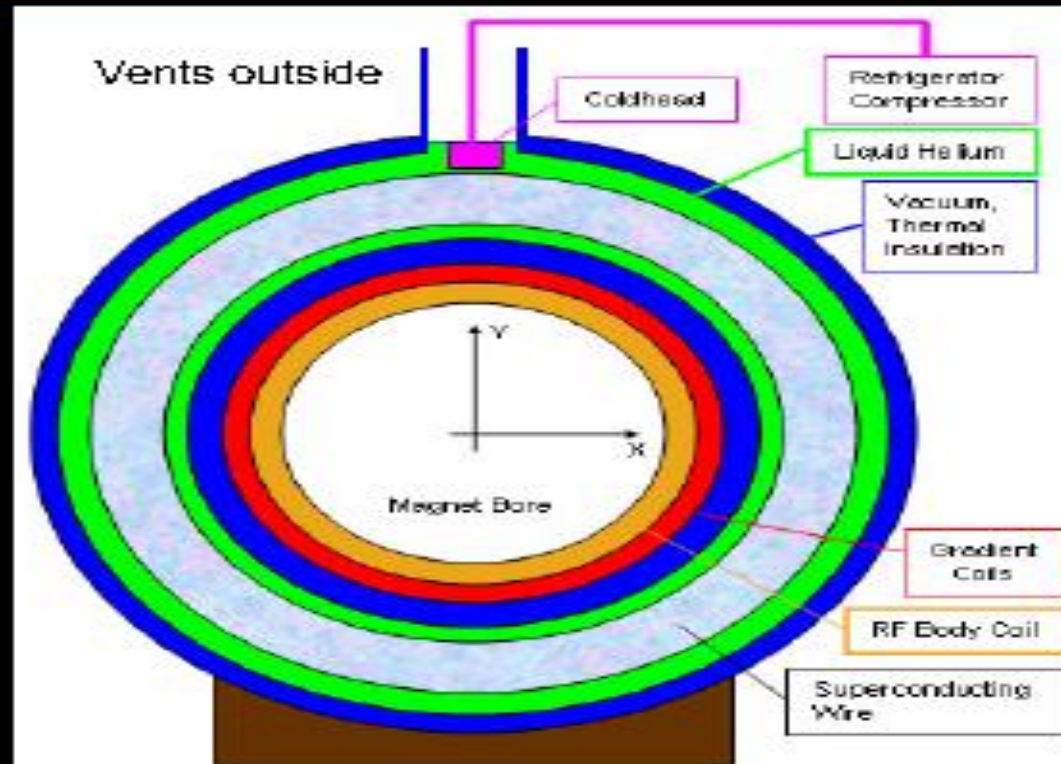
MRI physics

MR Physics



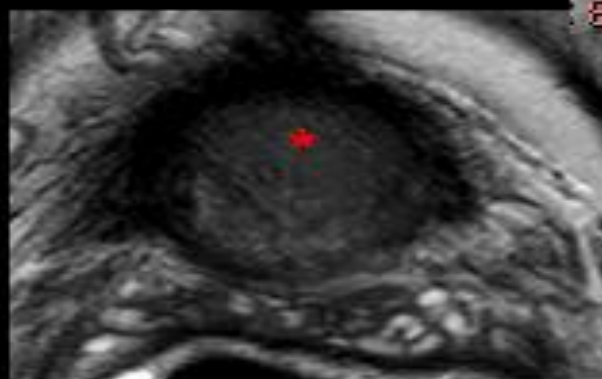
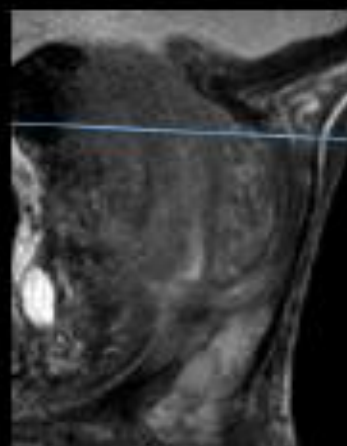
MRI anatomy

Anatomy of an MRI



MRI Imaging

1



801 - 18 >

64 y.o. with rising
PSA after multiple negative
biopsies

Midline base
anterior central
gland lesion

T2

T2 +

DWI +

DCE +

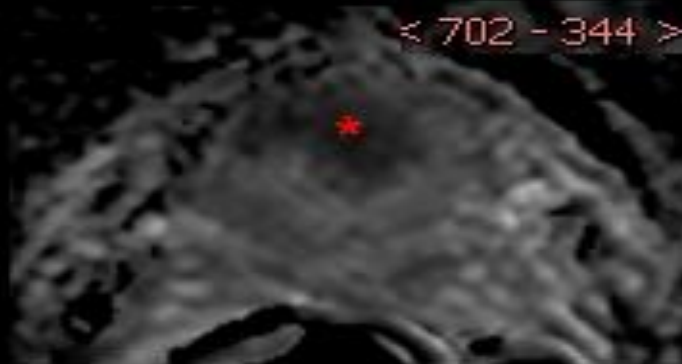
Highly suspicious

< 1231 - 215 >



DCE

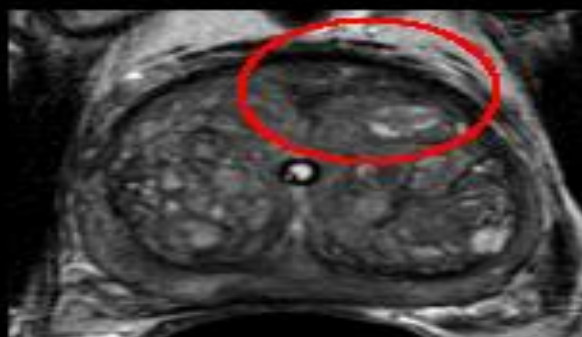
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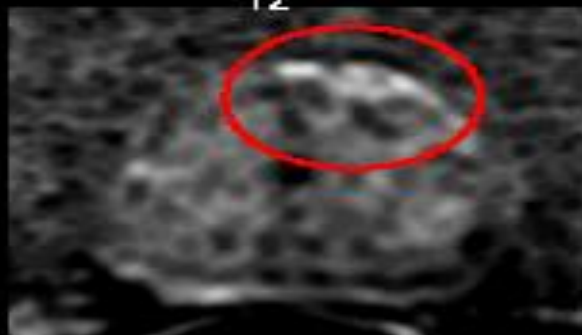
ADC map

Tumor detection

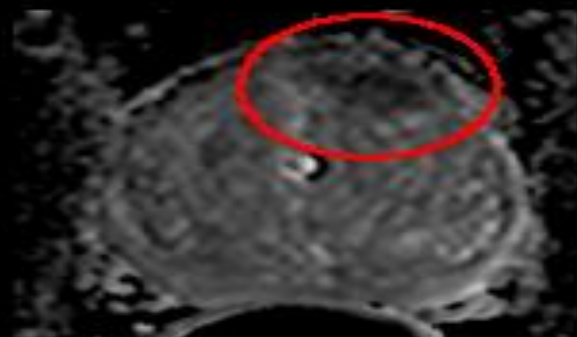
74-year-old man, PSA=7.33ng/dl, 2 prior negative TRUS guided biopsy



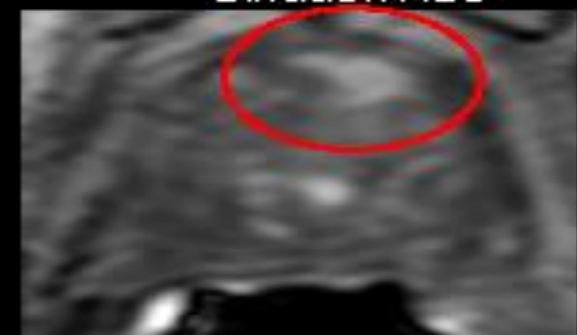
T2



Diffusion-high b-value



Diffusion-ADC



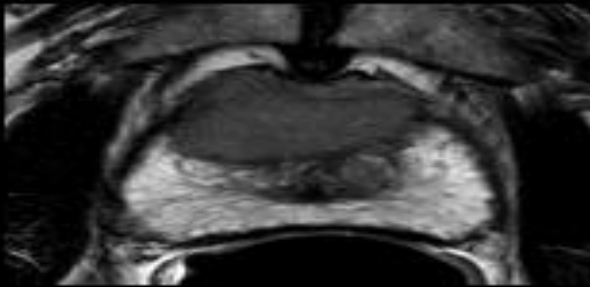
Dynamic contrast enhanced MRI

Left mid
anterior
TZ-1.8cm

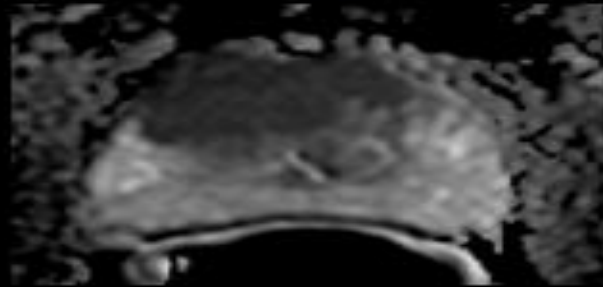
Gleason 3+4 (60% core involvement)

Prostate tumor

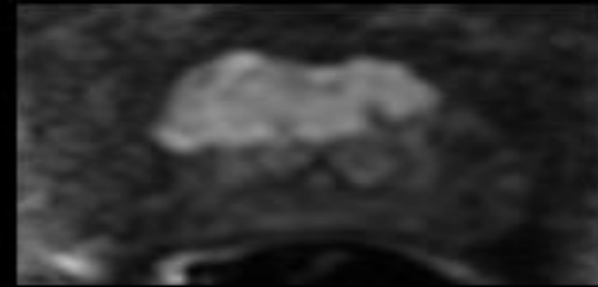
72-year old man with a serum PSA=38.6ng/dl with 3 prior TRUS guided biopsies



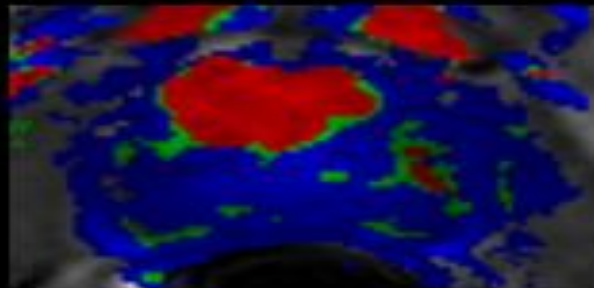
T2W MRI



ADC map



B=2000 DWI



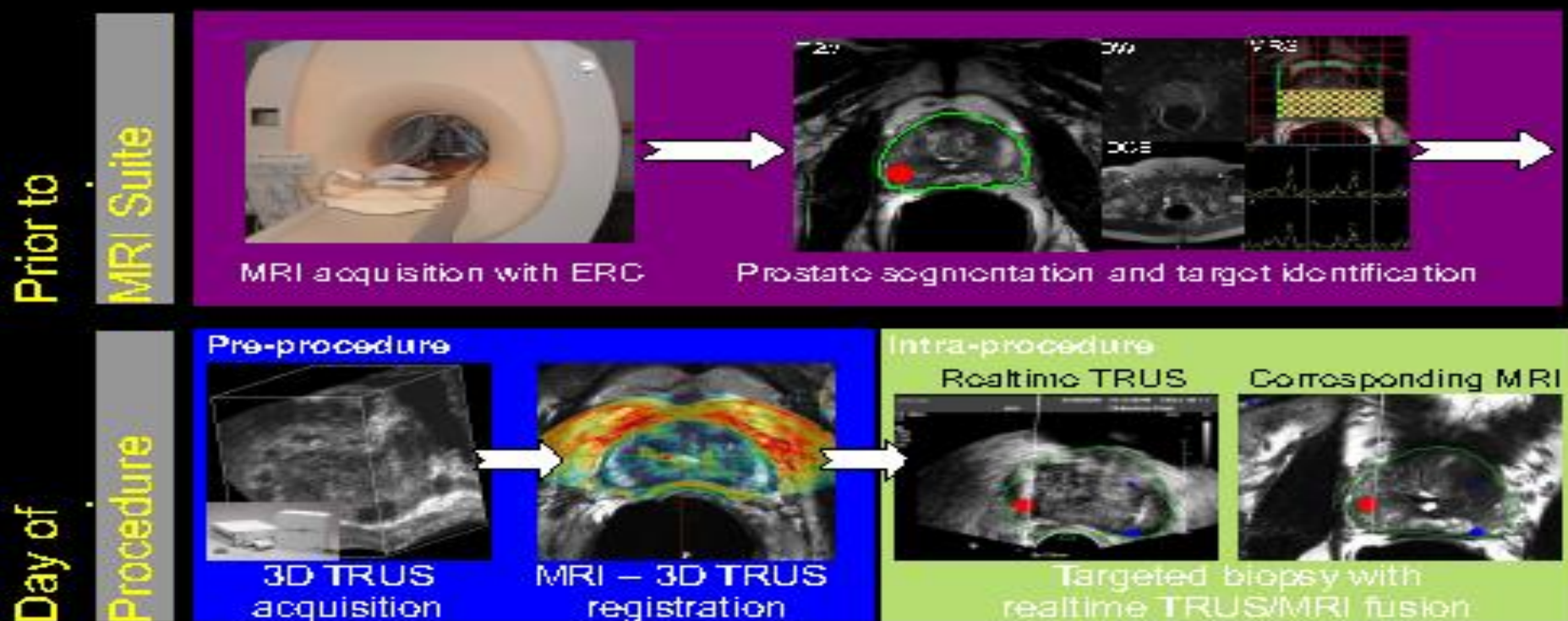
Color encoded
contrast
enhancement



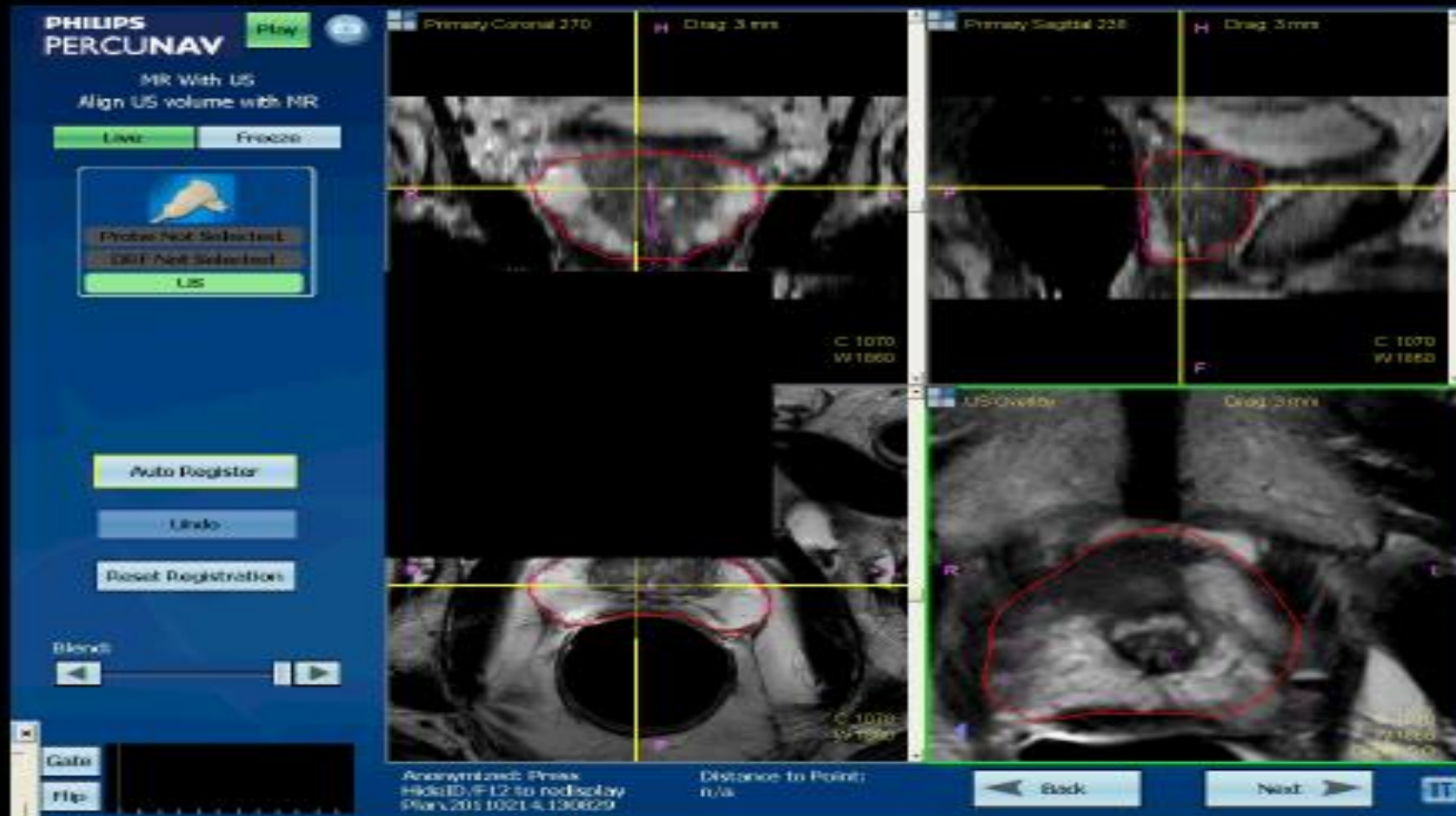
Brad Wood, MD

Prostate fusion

Prostate Fusion-targeted biopsy workflow



Prostate tumor Ultrasound fusion



Ultrasound fusion

Original Investigation

Comparison of MR/Ultrasound Fusion-Guided Biopsy With Ultrasound-Guided Biopsy for the Diagnosis of Prostate Cancer

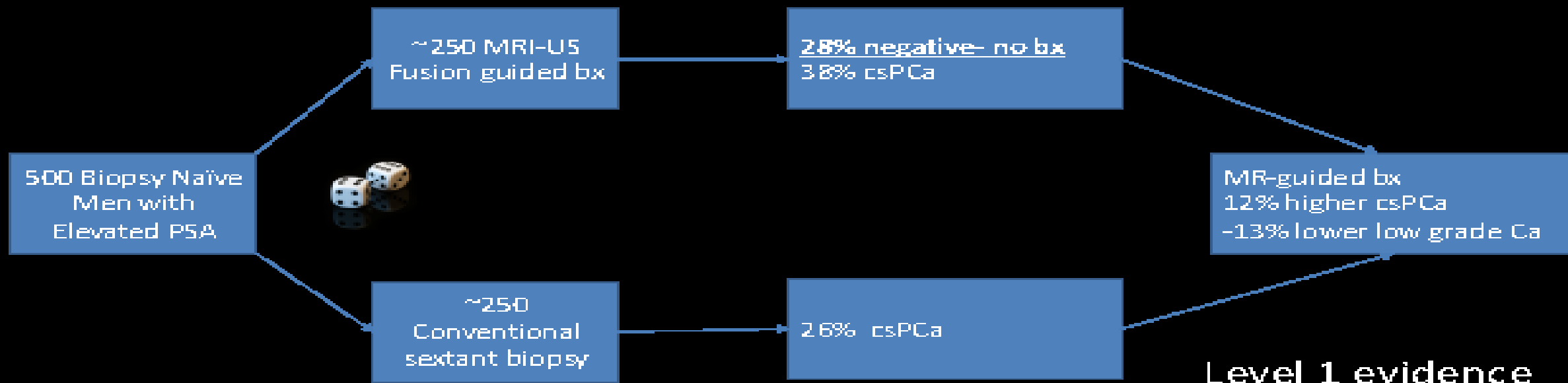
M. Minhaj Siddiqui, MD; Soroush Rais-Bahrami, MD; Baris Turkbey, MD; Arvin K. George, MD; Jason Rothwax, BS; Nabeel Shakir, BS; Chinonyerem Okoro, BS; Dima Raskolnikov, BS; Howard L. Parnes, MD; W. Marston Linehan, MD; Maria J. Merino, MD; Richard M. Simon, DSc; Peter L. Choyke, MD; Bradford J. Wood, MD; Peter A. Pinto, MD

- Key findings in over 1000 cases
 - 30% increase in the diagnosis of high-risk cancers using targeted biopsy
 - 17% decrease in the diagnosis of clinically-insignificant low risk cancers

Siddiqui M et al. JAMA. 2015

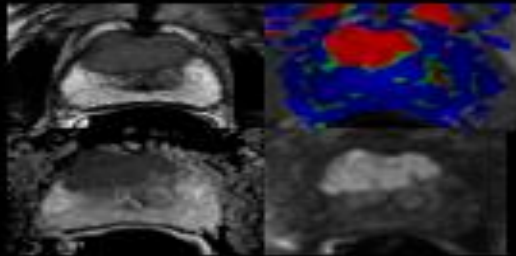
PRECISION study

PRECISION Study: 25 site study



Prostate imaging development

The Development of Prostate Imaging and Image Guided Biopsy 2000-2016



Multiparametric MRI 2000's



In gantry biopsy 2003-6



MRI-TRUS-GPS-2006



Clinical MR-TRUS Fusion 2008



Commercial MR-TRUS fusion
Devices 2013



World wide- Image
Guided Bx (IGB) 2018

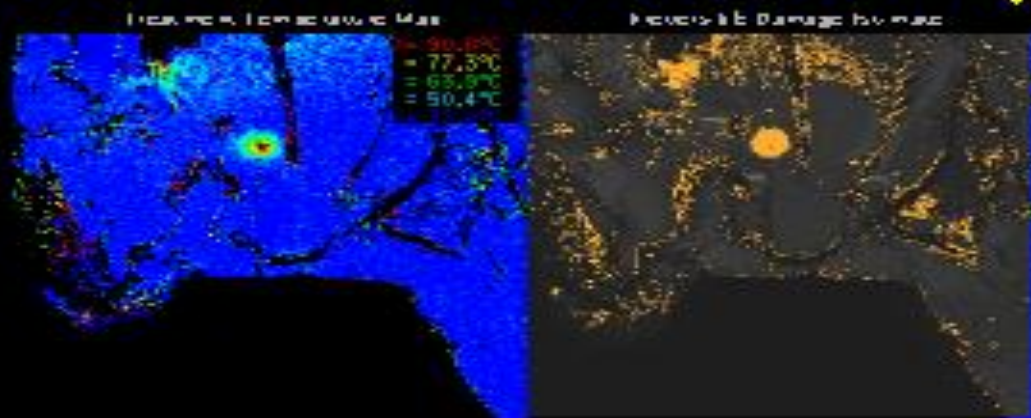
TRUS fusion industry

MRI TRUS Fusion Industry since 2010

MR-TRUS Fusion Software (Manufacturer)	US Image Acquisition	Method of Registration	Tracking System	Manipulation	Sampling Route	Targeting
Antaris (Eigen)	Manual	Non rigid	Mechanical Arm with encoders	Via Mechanical Arm	Transrectal	Prostate,ve
Biolot (GeoScan)	Manual	Rigid	Seppen with digital encoders	Via Seppen	Transrectal or Transperineal	Prostate,ve
BiopSoc (MedCom)	Manual	Rigid	Seppen with digital encoders	Via Seppen	Transperineal	Prostate,ve
RealTime Virtual Sonography (Hitachi)	Manual	Rigid	Electromagnetic	Freehand	Transrectal or Transperineal	Prostate,ve
UroNav (Invivo/Philips)	Manual	Rigid	Electromagnetic	Freehand	Transrectal	Prostate,ve
Urostation (Kodak)	Automatic	Non rigid	3D Ultrasound	Freehand	Transrectal	Re,transprostate,ve
Variscan (Varian Medical System)	Manual	Rigid	Seppen with digital encoders	Via Seppen	Transperineal	Prostate,ve
Virtual Navigator (Esaote)	Manual	Rigid	Electromagnetic	Freehand	Transrectal	Prostate,ve

Laser ablation

Focused Laser Ablation-Local Therapy



Test dose
3.75 W for 34 sec

Laser Doses
12 W for 32, 25 and 63 sec

Damage 18 mm by 17 mm

Temperature safety limits
were set to protect the
urethra, shutting down the
laser power automatically.



Baris Turkbey



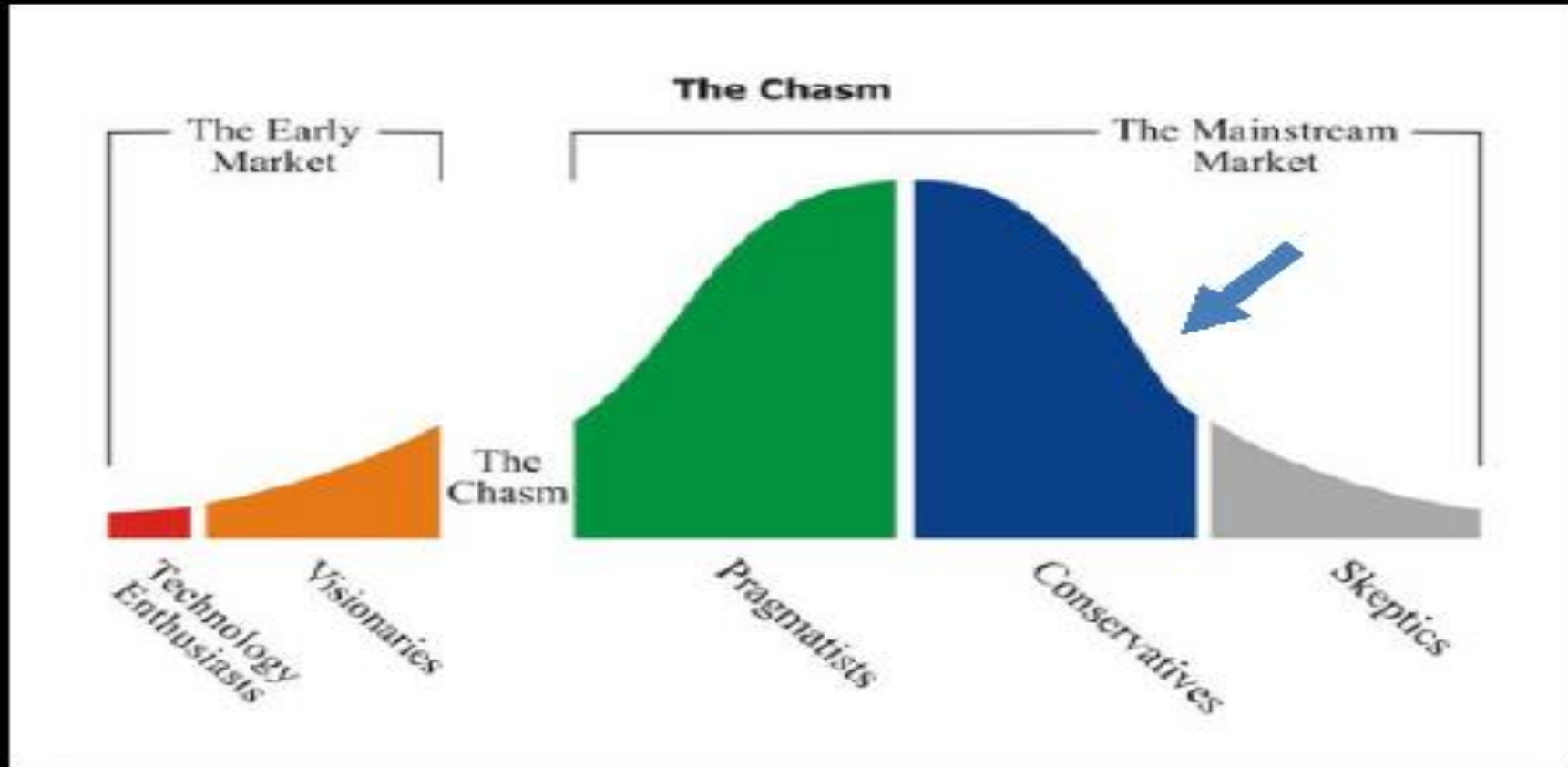
Peter Pinto



Brad Wood



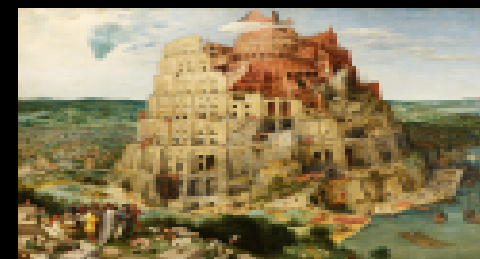
Cancer views



Lack of standards

Lack of Standards: Prostate Imaging, Reporting and Data System Version 2 (PI-RADSv2)

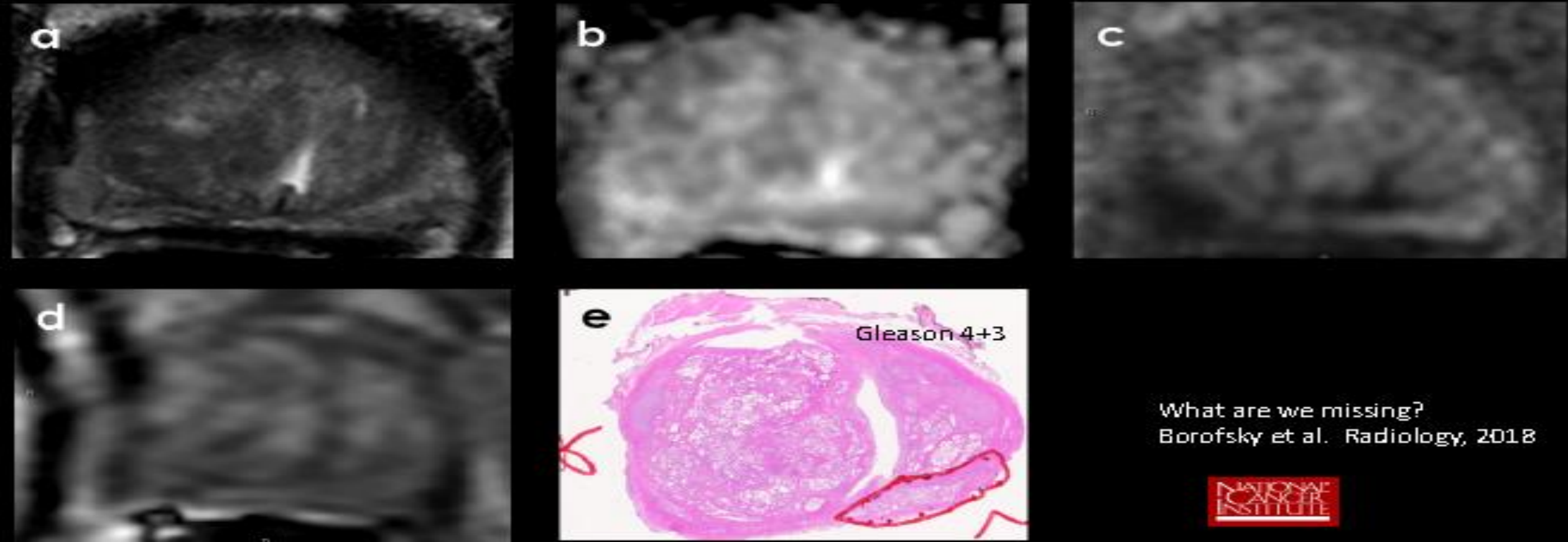
- Each lesion is scored PI-RADS 1 to 5
 - Rules:
 - Score each T2W, DWI, DCE separately
 - In PZ DWI predominates
 - In TZ T2 predominates
 - DCE MRI helps in equivocal cases
 - What does a PIRADS score mean:
 - Likelihood of diagnosing a Clinical Significant (\geq ISUP2) Prostate Cancer
 - PIRADS 5 ~60-70%
 - PIRADS 4 ~40-50%
 - PIRADS 3 ~15-20%



The Tower of Babel by
Pieter Bruegel the Elder
(1583)

False negative rate

The MR negative lesion: False negative rate = 5-20%



What are we missing?
Borofsky et al. Radiology, 2018

MR-based mold

Patient-Specific MR-based Mold

Shah et al. Rev Sci Instrum. 2009 Oct; 80(10):104304 (Research Highlight for Oct'09 issue)

T2W



Printed
at CIT, NIH



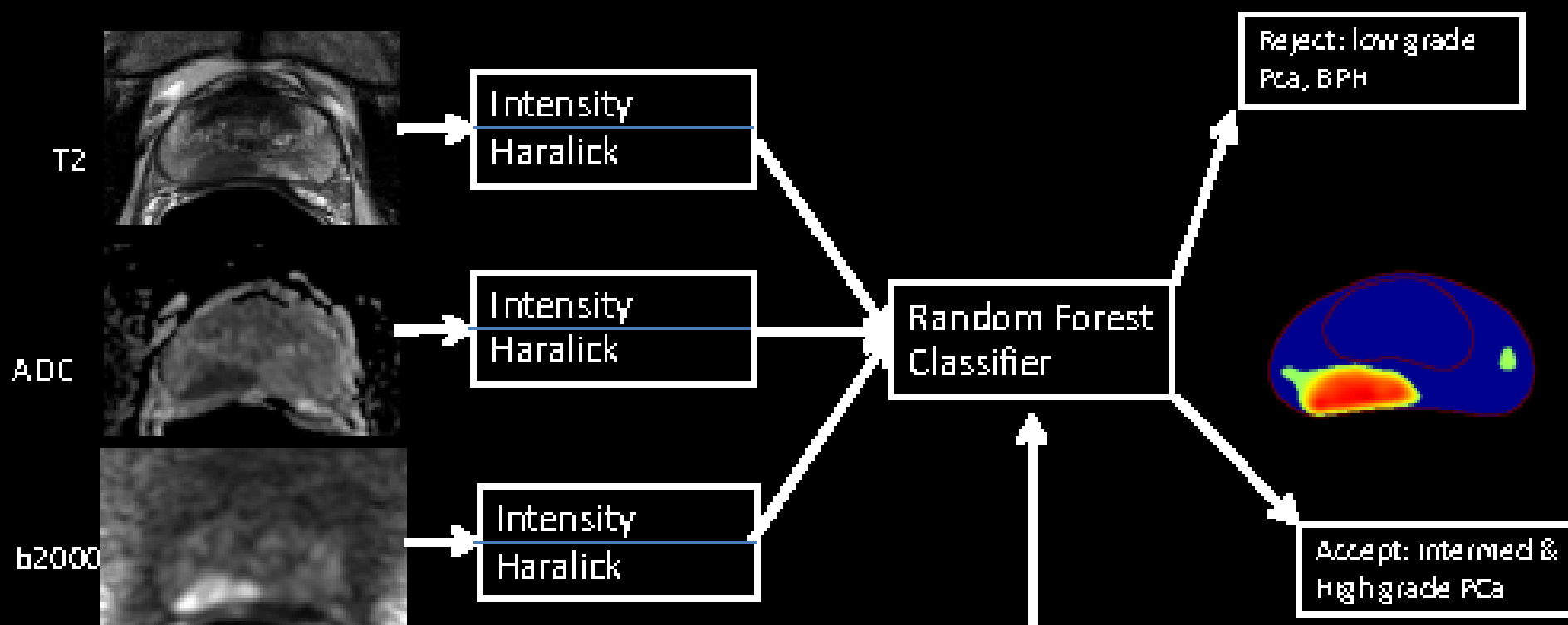
Tissue Blocks Obtained from Prostatectomy Specimen



Marcelino Bernardo

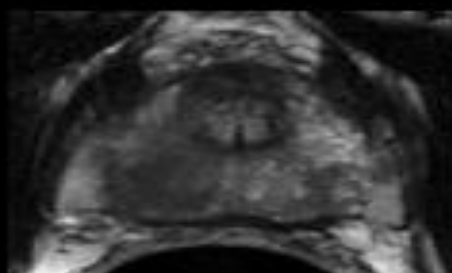
Artificial intelligence sensitivity

Is Artificial Intelligence More Sensitive?

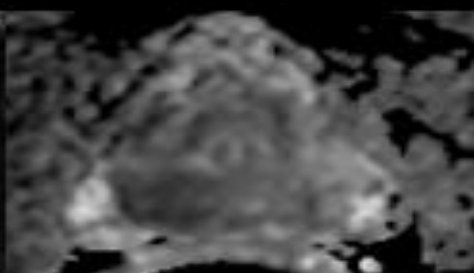


AI outperforms humans

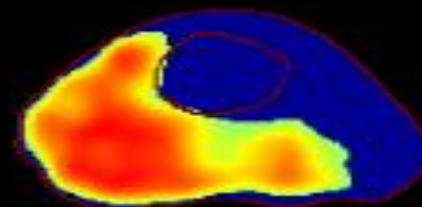
AI Outperforms Trained Human Readers in Defining Lesion Contours



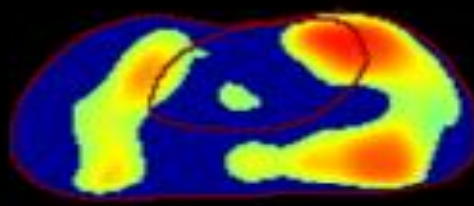
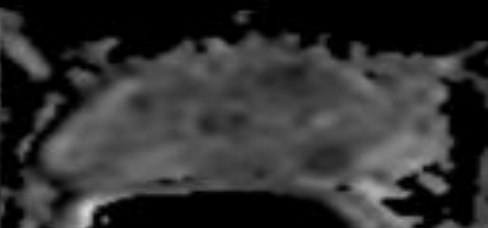
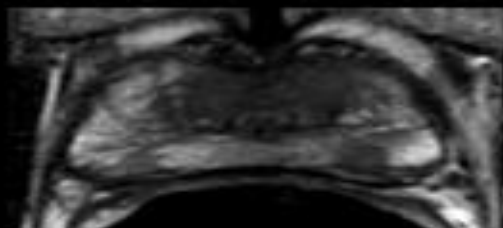
T2W



ADC



CAD



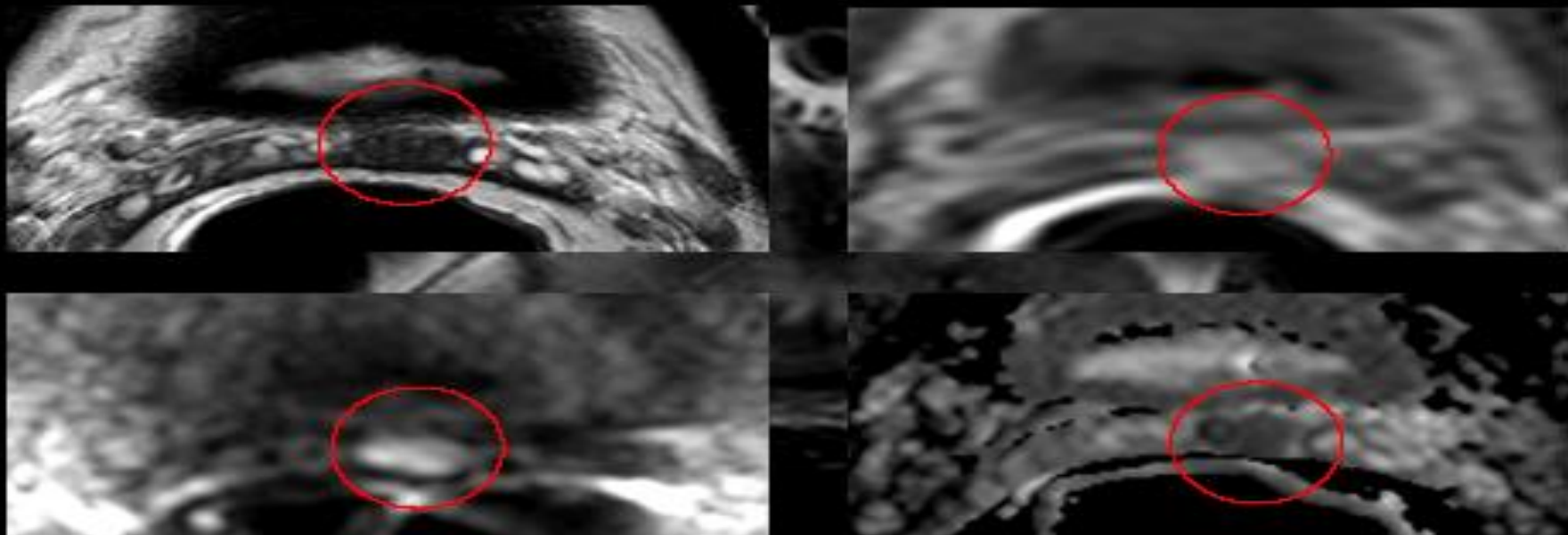
MRI summary

Prostate MRI Summary

- MRI-US Fusion biopsy detects more clinically significant cancers and fewer insignificant cancers
- Level one evidence supports MR guided biopsy in lieu of sextant biopsies
- Concern over “missed” csPCa on MRI can be mitigated by
 - Continued observation
 - Consideration of clinical factors (PSA density)
 - Computer Aided Diagnosis (CAD)

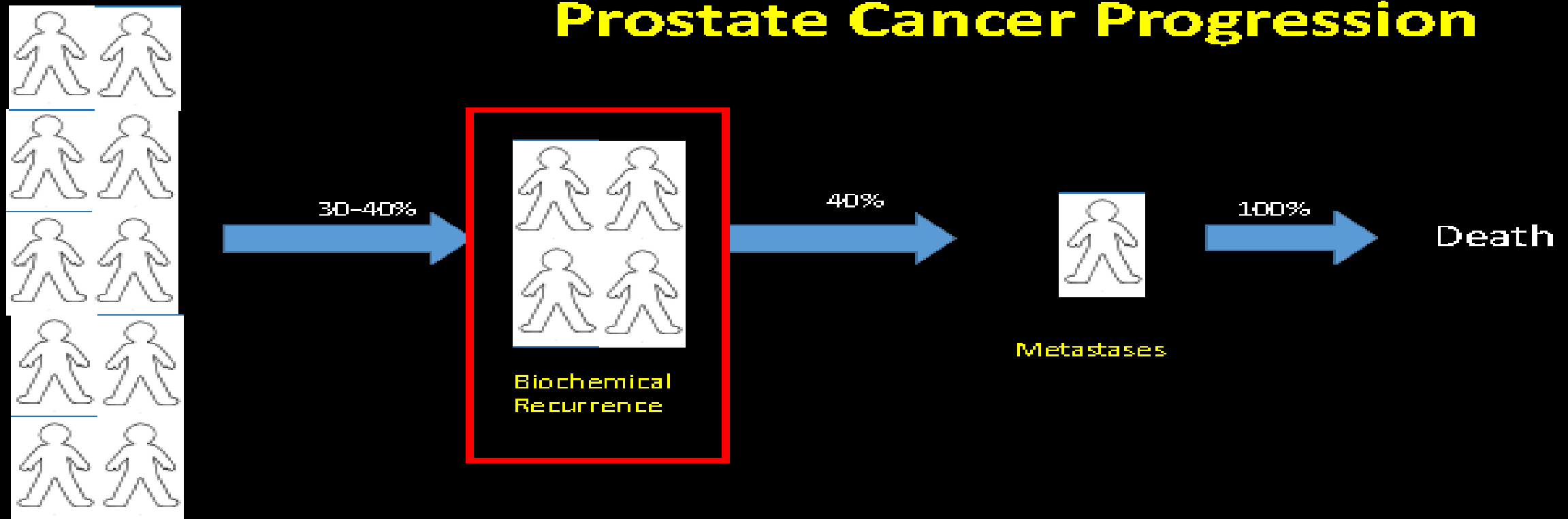
Brachytherapy

61 year old male, PSA=5.54ng/ml S/P
brachytherapy 5 years ago



12 core systemic bx negative
Gleason 4+3 Pca in left SV

Prostate cancer progression

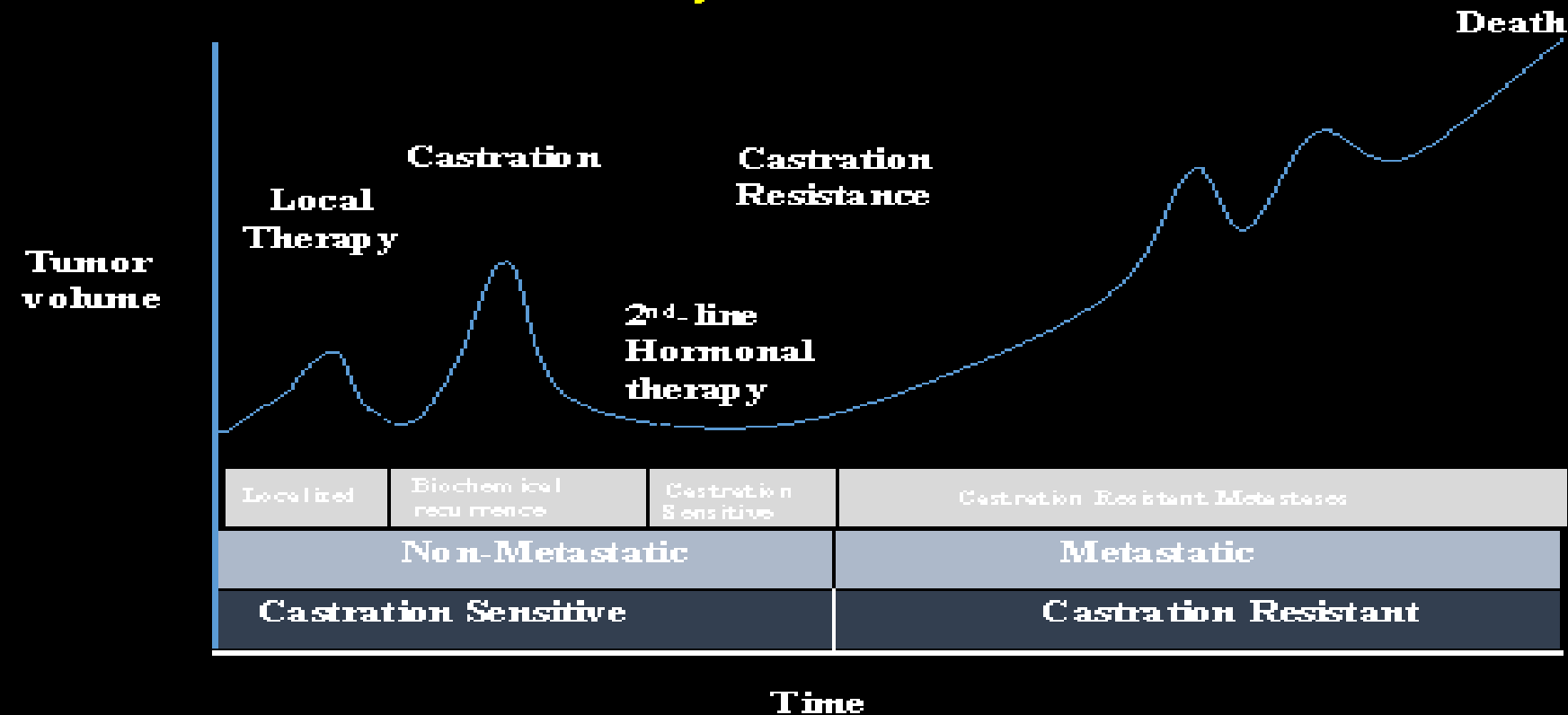


Primary Treatment

Ken Pienta, PCF 2017
Howard Scher JCO 2005

Prostate cancer history

Natural History of Prostate Cancer



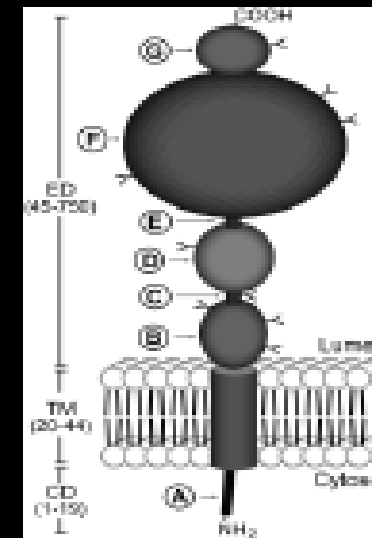
Prostate specific membrane antigen

Prostate Specific Membrane Antigen (PSMA)

- PSMA (prostate specific membrane antigen) is a transmembrane protein, which is highly expressed in many prostate cancers, particularly high grade cancers.
- Urea-based compounds have high affinity for the enzymatic domain of PSMA and are used for PET imaging



Marty Pomper MD PhD

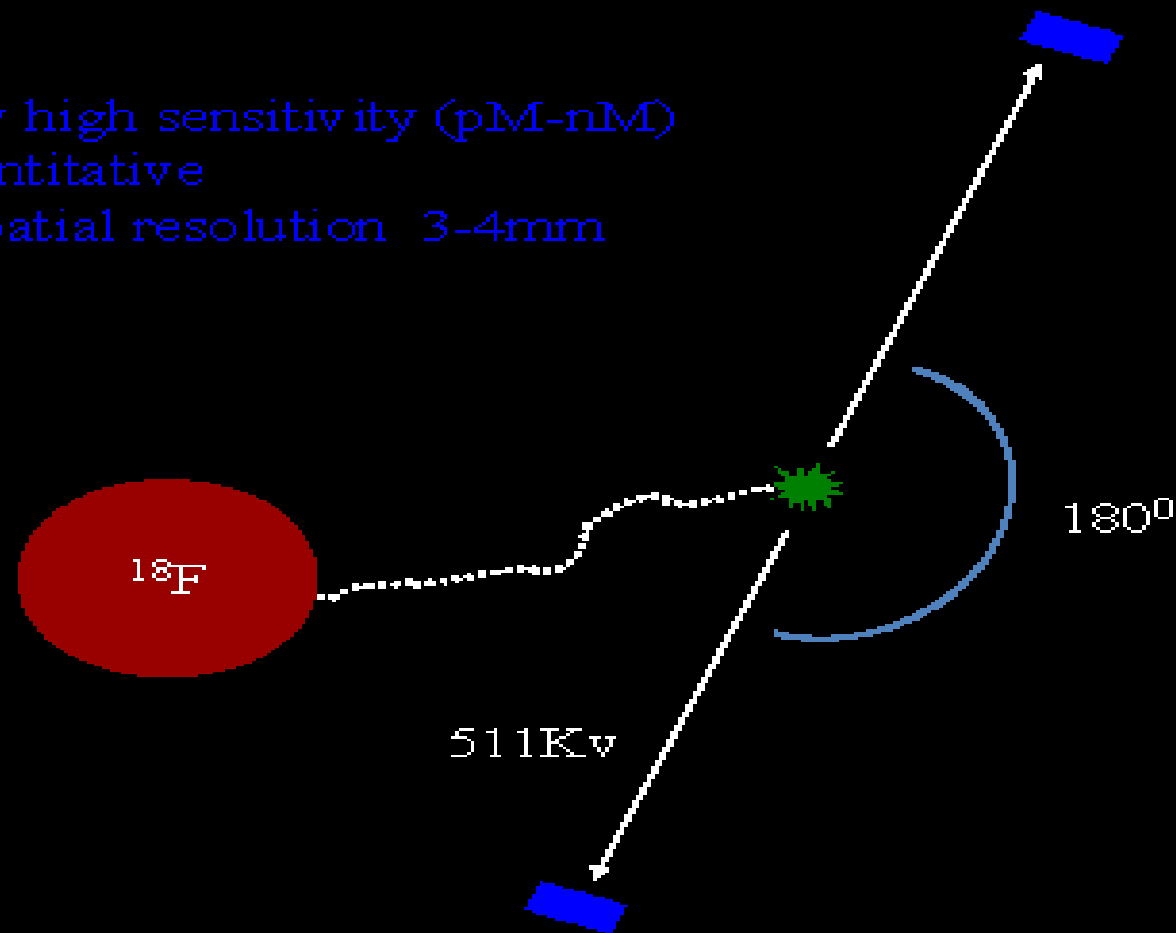


PSMA receptor

<http://map.onlinelibrary.wiley.com/doi/10.1002/psma.201700001>

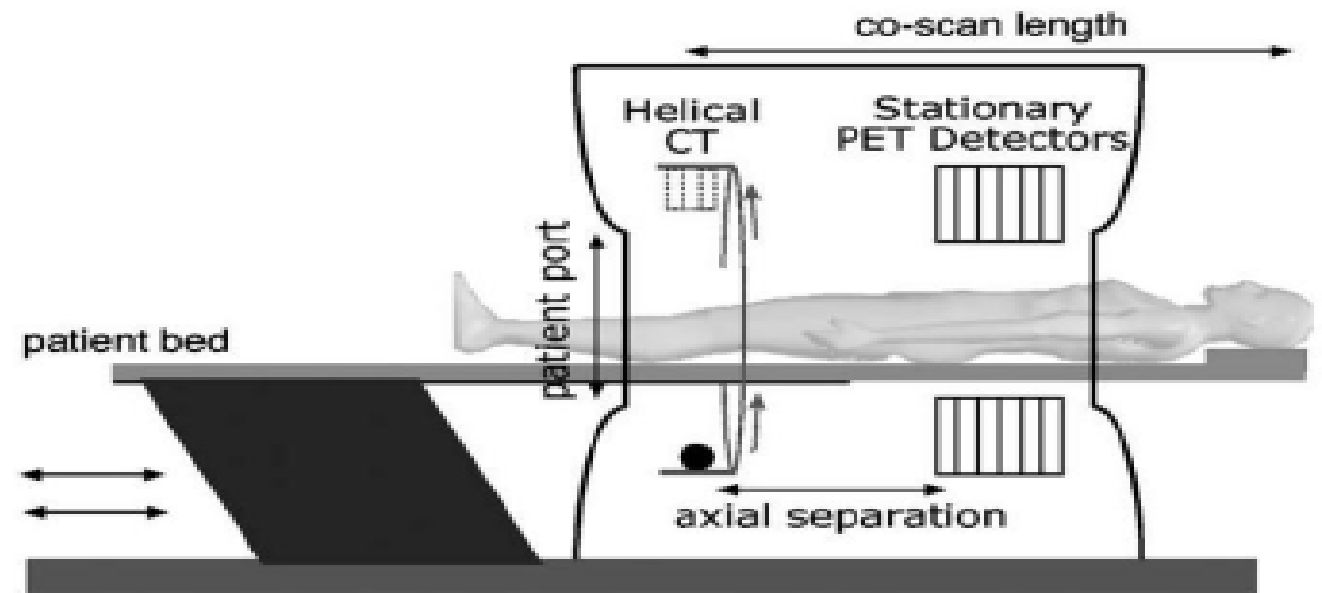
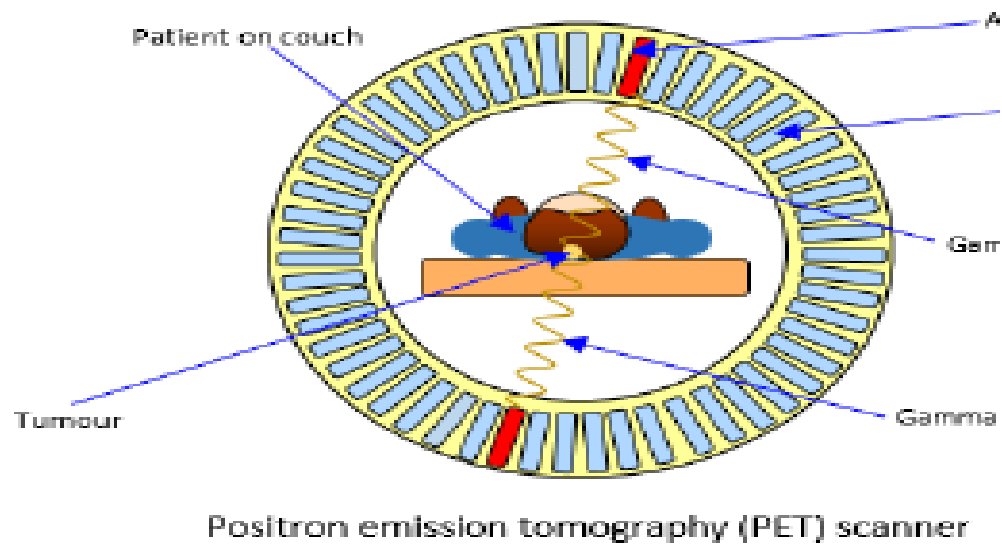
^{18}F

Very high sensitivity (pM-nM)
Quantitative
 \pm Spatial resolution 3-4mm



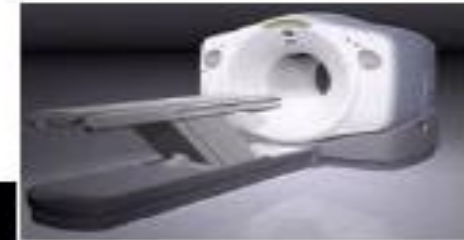
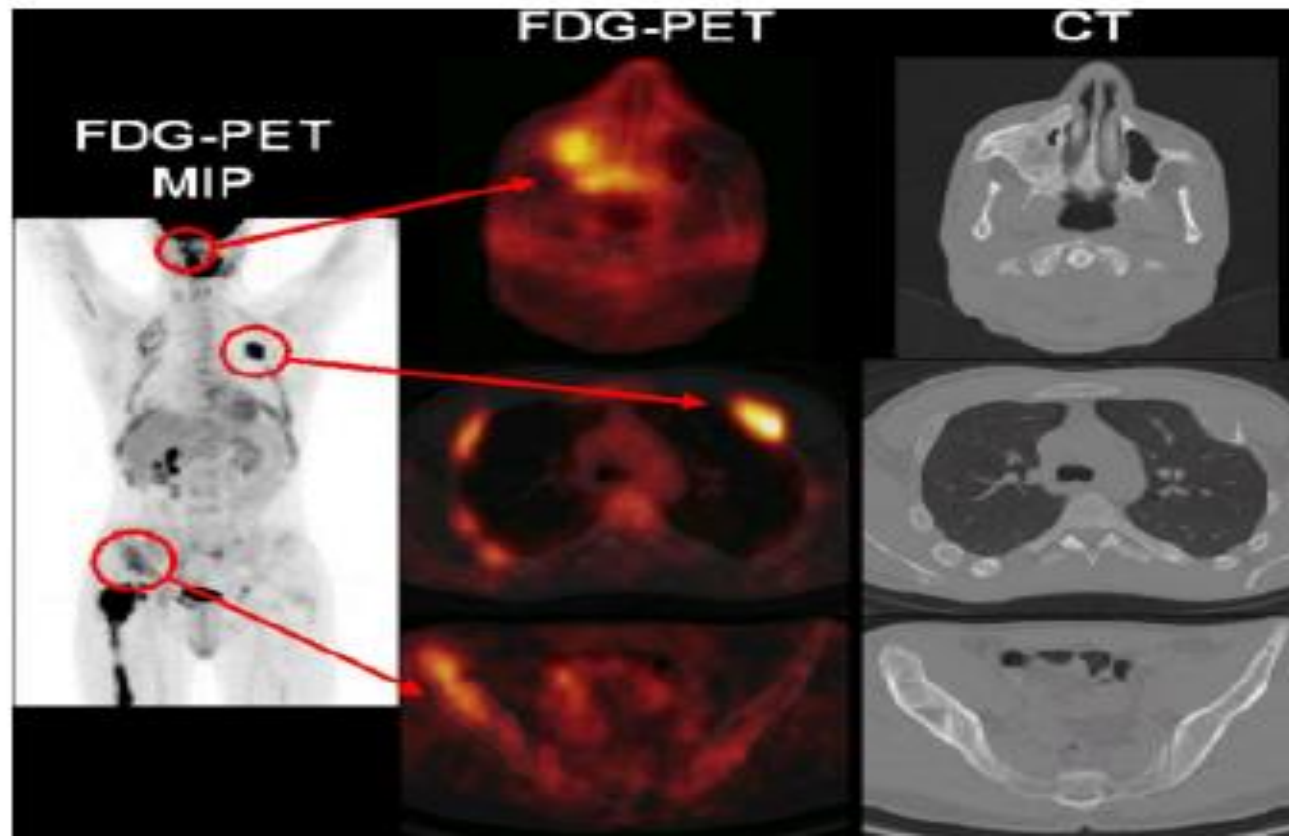
PET/CT camera

PET/CT Camera

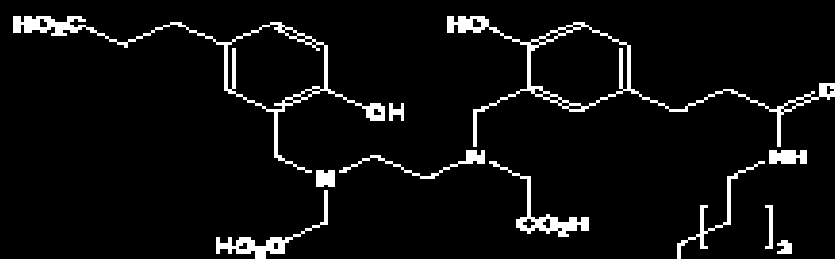


PET-CT scanners

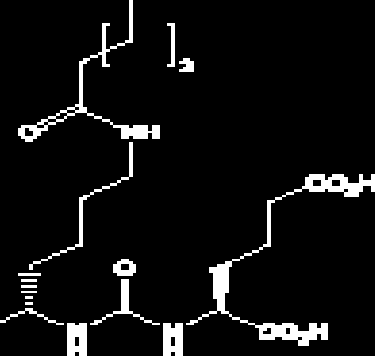
PET-CT scanners



NeXT project ligands

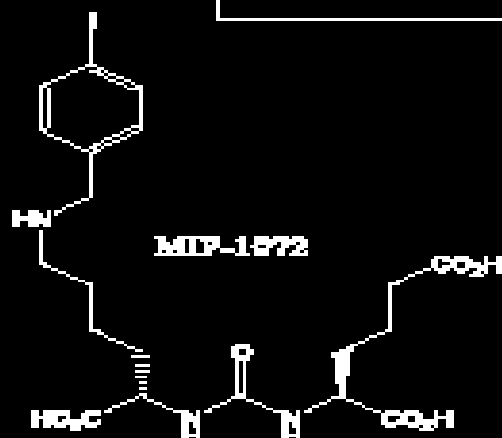
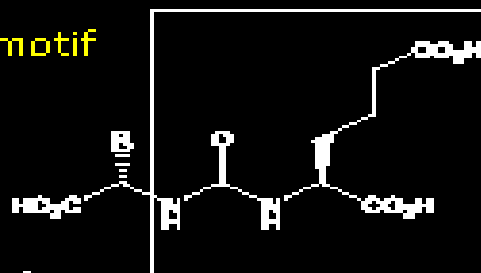


Glu-NH-CO-NH(Lys)(Ala)-EBED-CO

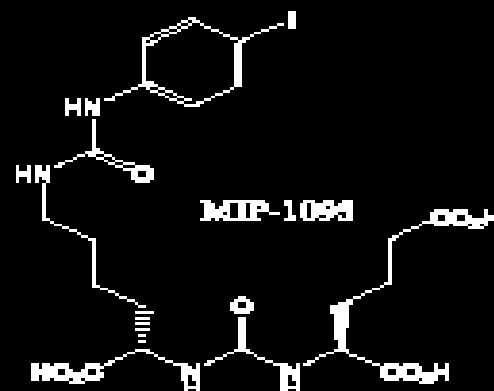


Urea binding motif

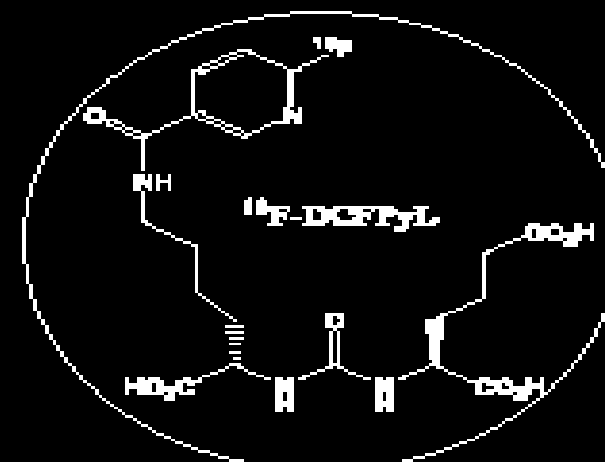
In square, common to all structures



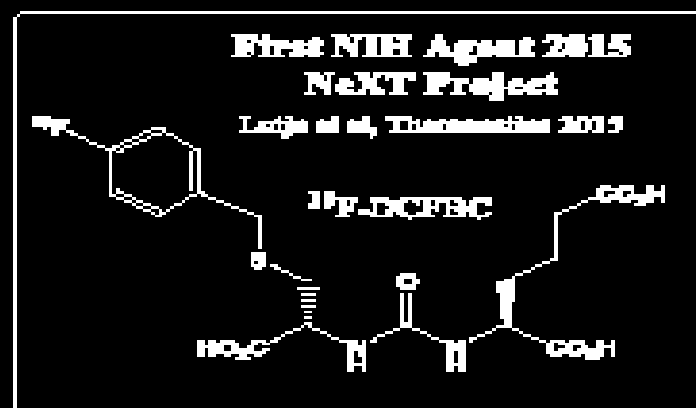
MIP-1072



MIP-1094



Second NIH Agent 2017
Commercialization underway

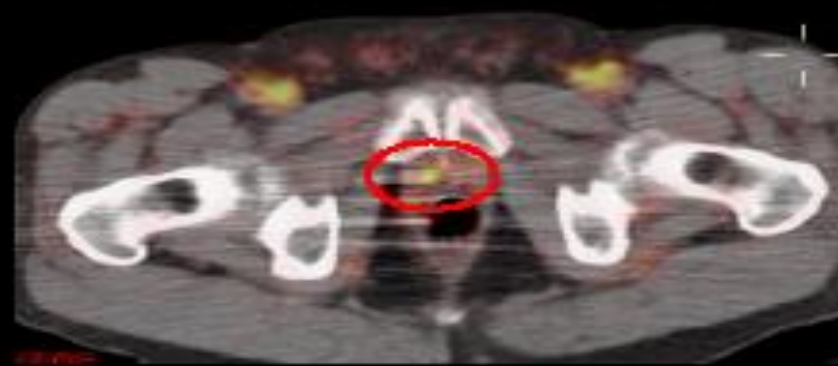
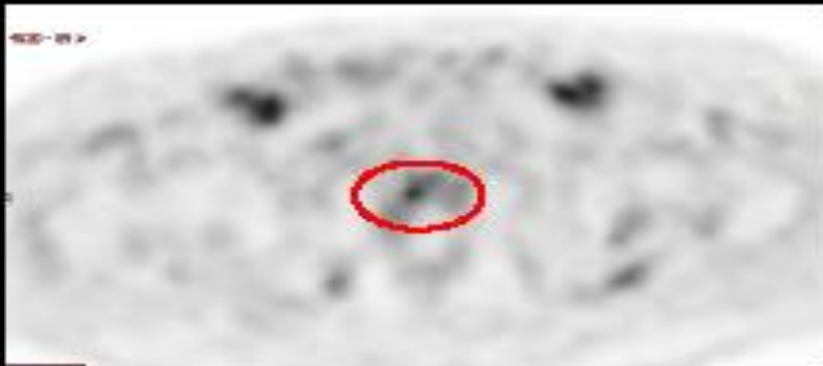
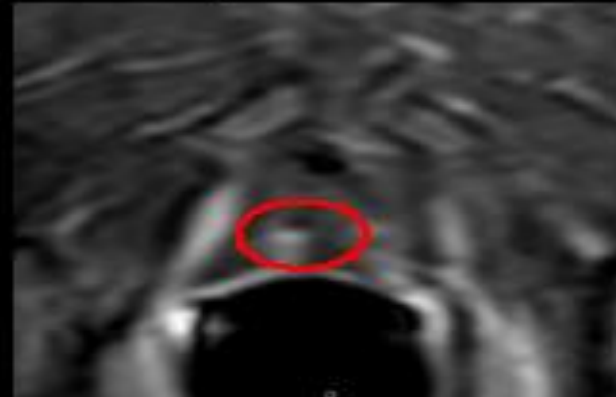
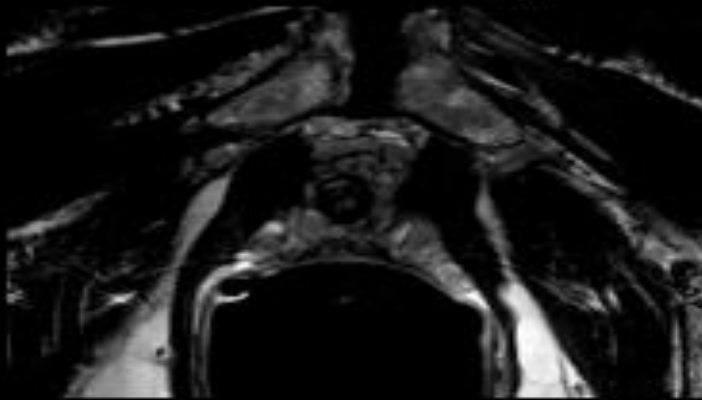


First NIH Agent 2015
NeXT Project

Loije et al, Theranostics 2015

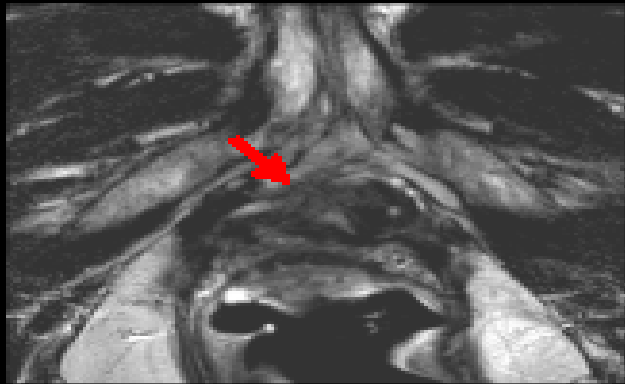
Case report

69-year old man, S/P RP 6 years ago, PSA=0.25ng/ml
(¹⁸F-DCFBC PET)



Recurrent disease

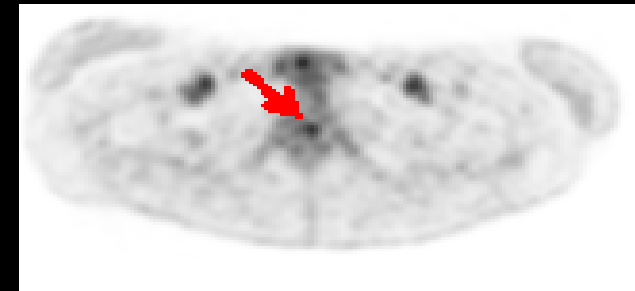
Recurrent disease detected by ^{18}F -DCFBC



Axial T2W MRI



Sagittal
 ^{18}F -DCFBC PET

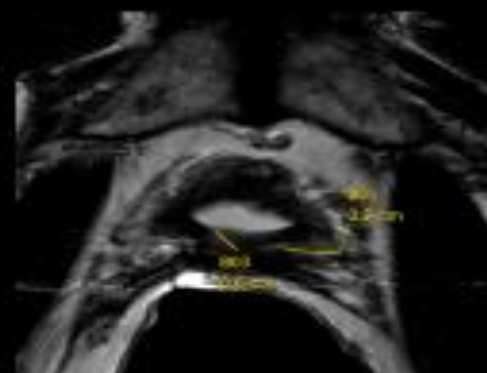
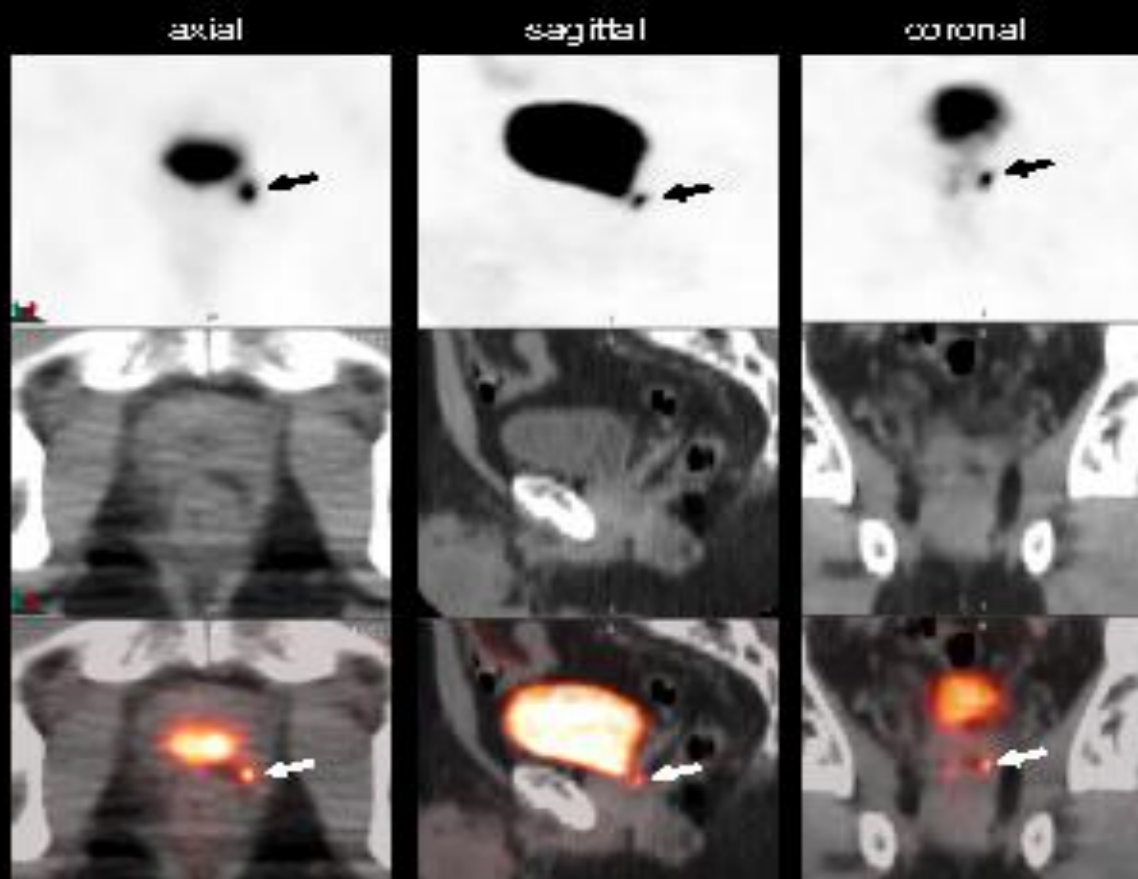


Axial ^{18}F -DCFBC
PET

58-year old man, S/P radical prostatectomy, PSA=1.4ng/ml
with recurrence at anastomosis

Local recurrence

Local Recurrence: DCFPyI PET/CT



Liza Lindenberg



Esther Mena

Status post-prostatectomy (2007) Recent PSA (10/02/17) = 1.29 ng/mL.

Local recurrence

Local Recurrence DCFPyL PET/CT



Protocol 17-C-0109_BCR; DCFPyL #006 s/p Prostatectomy in 2013 (multifocal carcinoma, Gleason score 3+3, negative margins (staged pT2c pNx). Salvage radiation therapy 70.2 Gy from 03 to 05 2014. Post-radiation PSA nadir was 0.040 in 5/2015. Rising with PSA, now 3.09 ng/mL on 09/22/2017



Deb Citrin

Traditional imaging

Traditional Imaging of Prostate Cancer

- Transrectal Ultrasound (TRUS) for guiding prostate biopsies
- Computed Tomography (staging)
- Tc-99m MDP Bone Scans
- Plain radiographs of the bone

Computed tomography

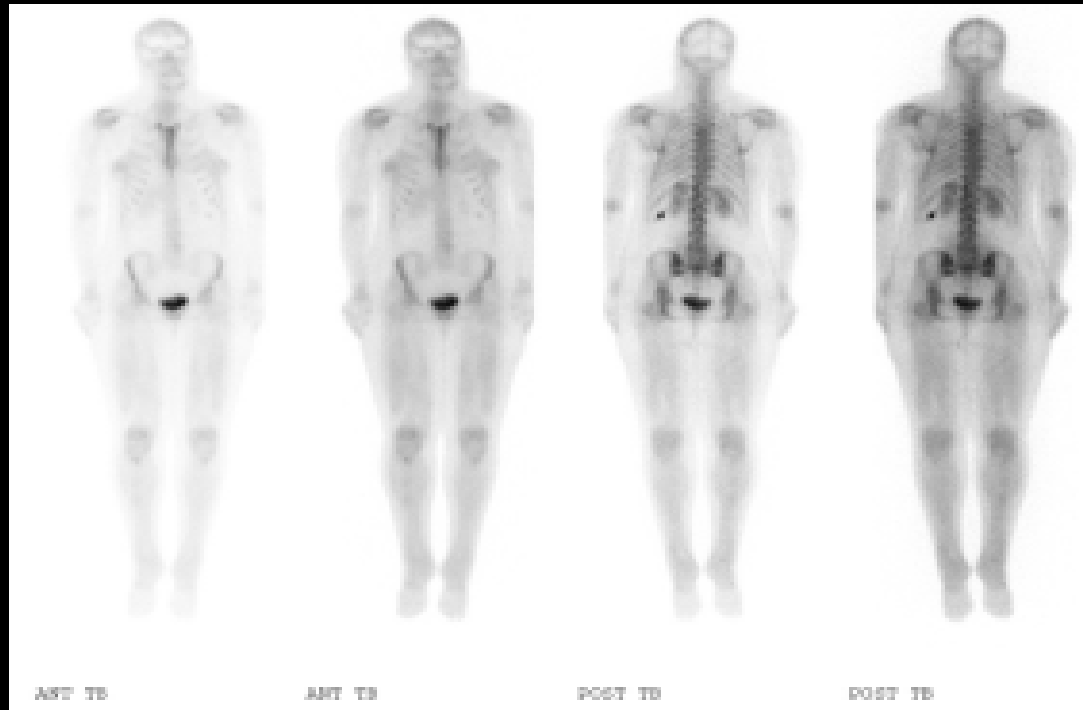
Computed Tomography



- For nodal staging, based on diameter/shape of the node
 - False negatives: small nodes harboring cancer
 - False positives: large inflammatory nodes
- For bone staging:
 - Osteoblastic lesions: benign or malignant?
 - Is disease live or dead?

Bone scan

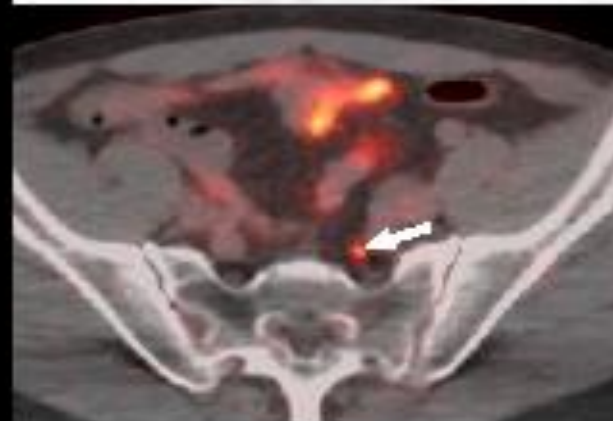
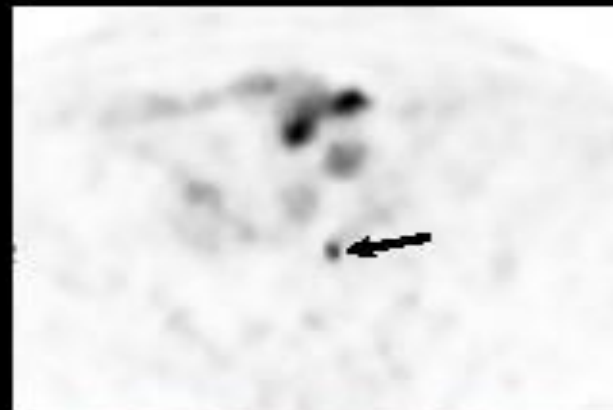
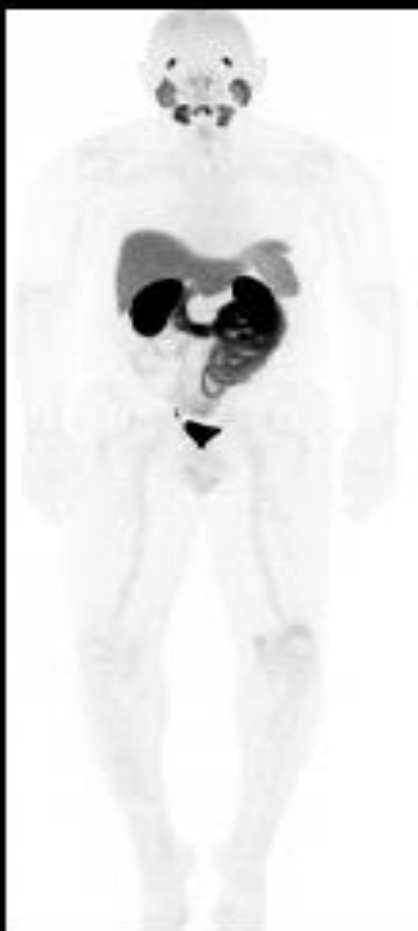
Bone Scan



- Insensitive for small bone lesions
- Non specific (benign lesions)
- Difficult to localize lesions
- Takes 3-5 hours

Lymph node metatases

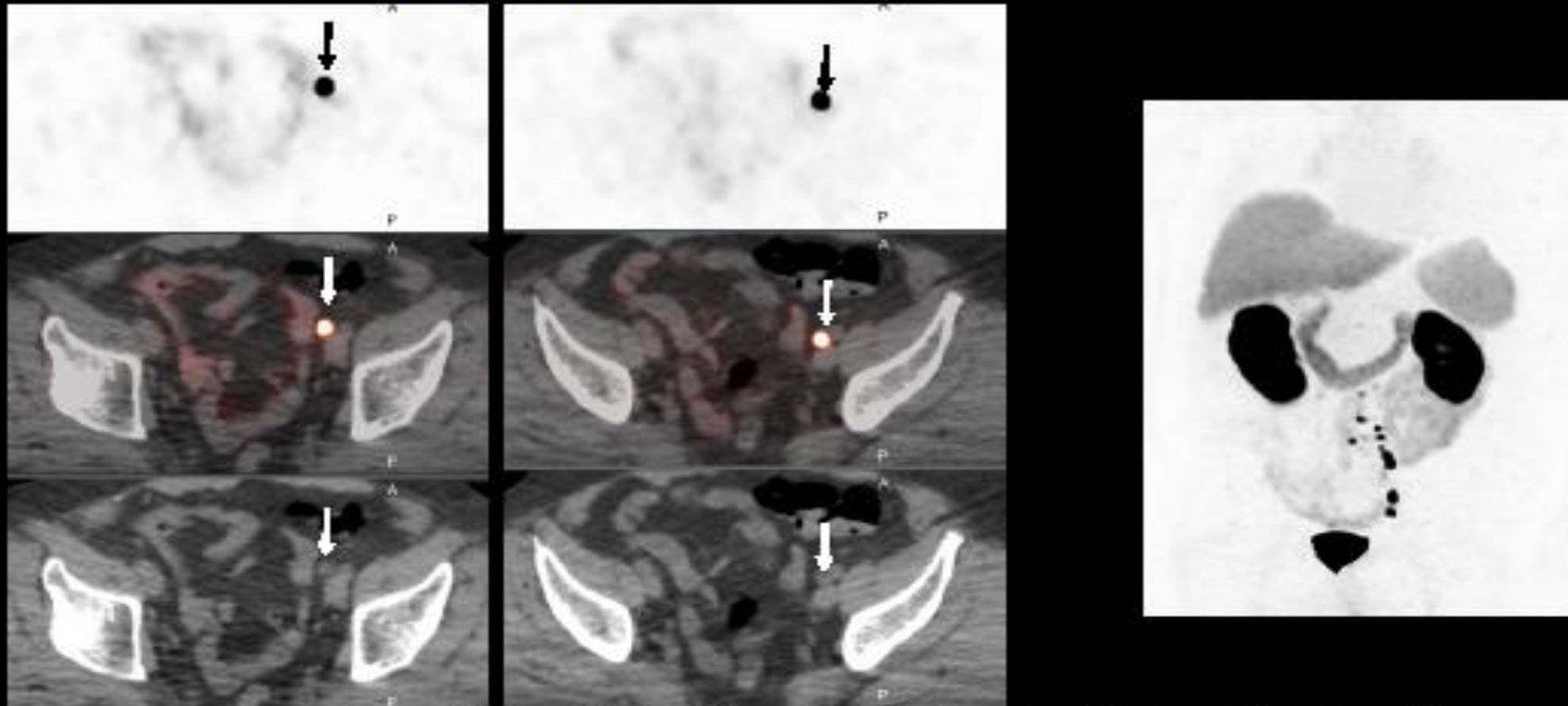
Lymph Node Metastases



Status post-radical prostatectomy (03/2017), pT3a pN0 M0, Gleason 4 + 3 with tertiary pattern 5 with extraprostatic extension. PSA (11/29/2017) = 0.40 ng/mL

Lymph node recurrence

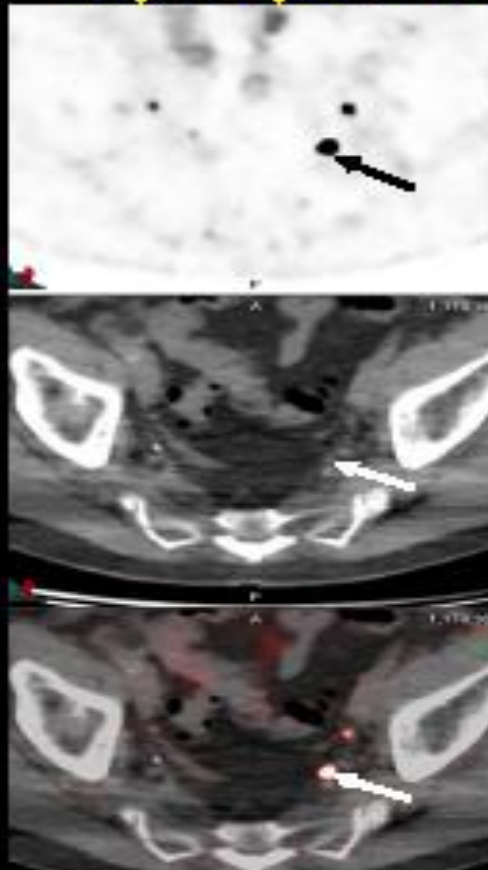
Lymph Node Recurrence



72 year old male with prostate adenocarcinoma, s/p prostatectomy (2009) stage IIb:
pT2cN0 Gleason 7 (4+3) PSA (01/09/2018) = 7.42 ng/mL.

Lymph node and bone metastases

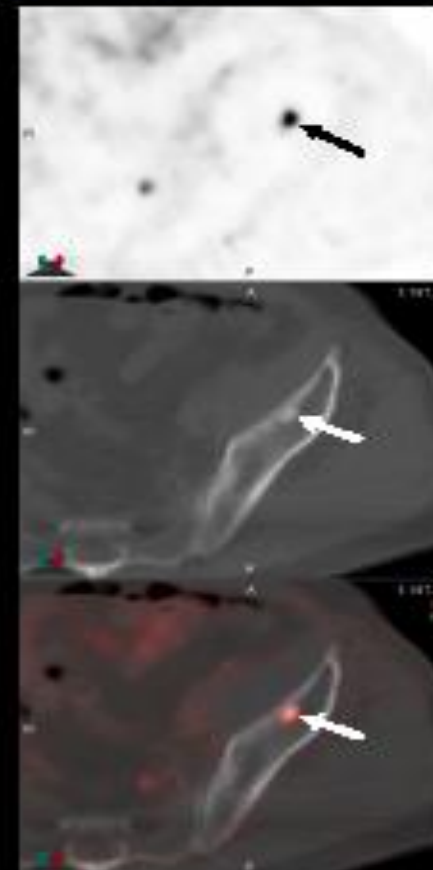
Lymph node and bone metastases



DOT-Py₂ and venous phase CT image of right iliac lymph node (7 mm)



DOT-Py₂ and subacute phase CT image of sacral lymph nodes



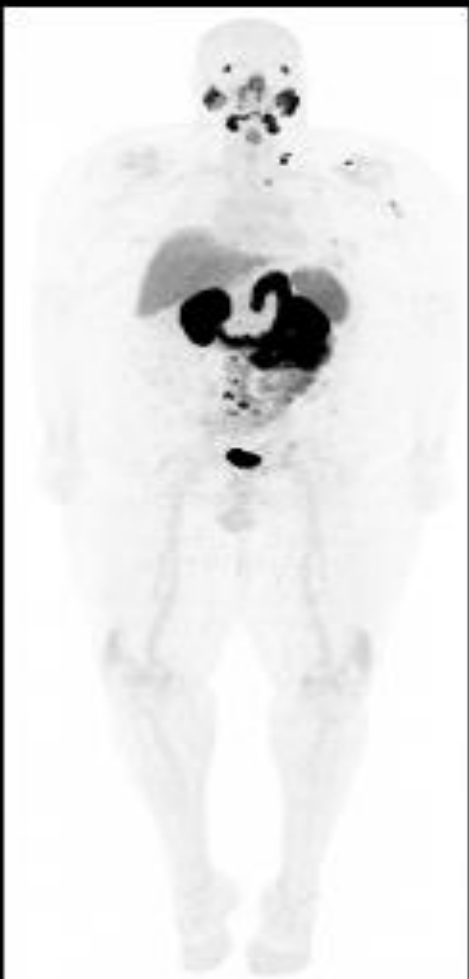
DOT-Py₂ and venous phase CT image of right iliac bone lesion (11 mm)

s/p prostatectomy
08/2010, Gleason
4+3=7 with SV
extension, negative
margins.
PSA (11/29/2017)=
13.29 ng/mL

Case report

17C-0089 - DCFPyL # 0011 (RG) 08/17/2017- PSA= 5.61 ng/mL

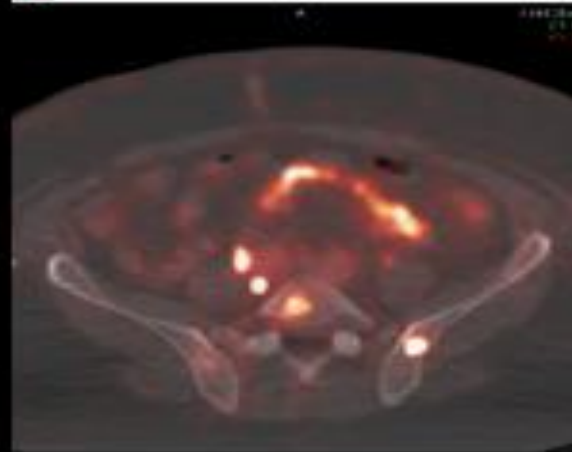
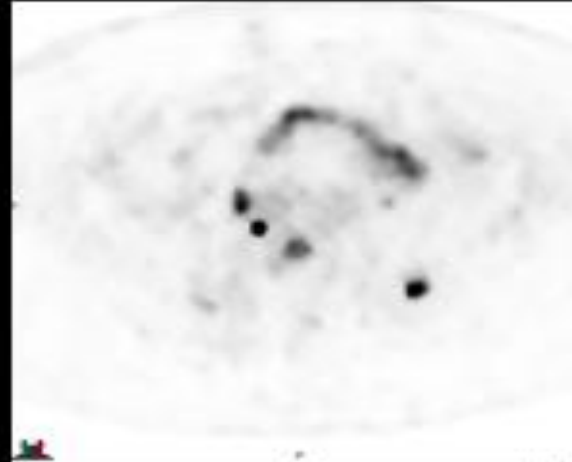
DCFpyL PET/CT



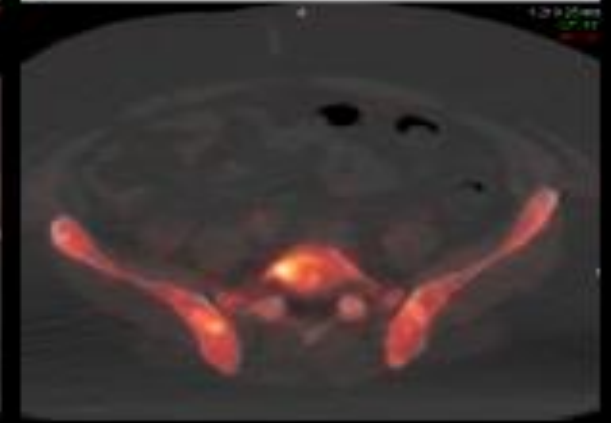
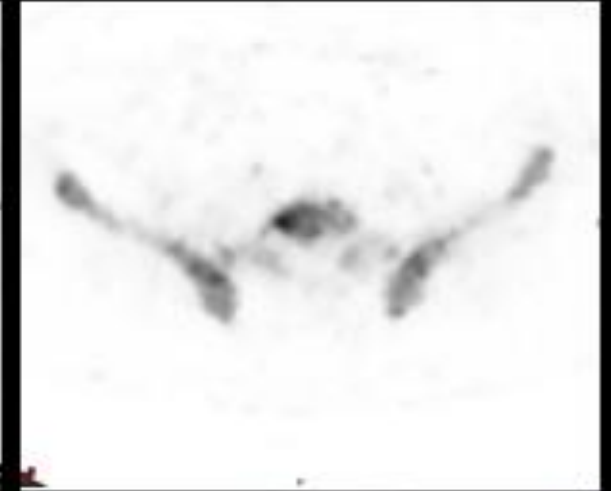
NaF PET/CT



DCFpyL PET/CT



NaF PET/CT



Case report

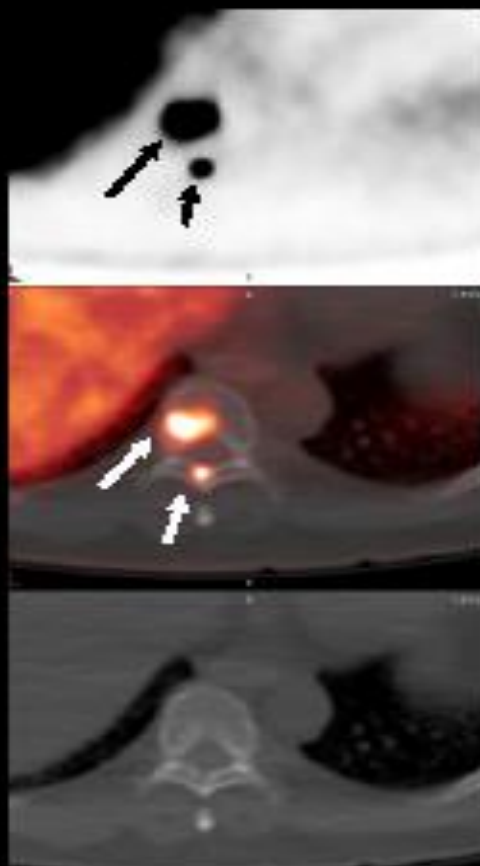
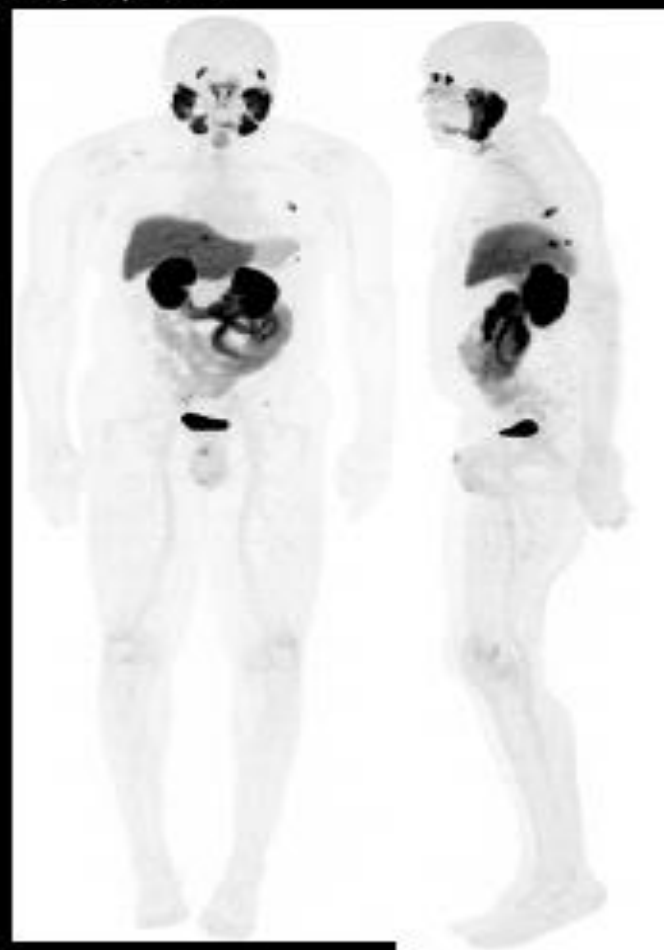
Protocol 17-C-0109

BCR; DCFPyL #032

^{18}F -DCFPyL PET/CT imaging

01/18/2018

55 year old male with intermediate-risk prostate cancer (GS 3+3, PSA 14 [pre-tx], cT1c, s/p EBRT + LDR brachytherapy implant + short-term ADT [completion of therapy 05/2015], who presents with biochemically recurrent disease [PSA doubling time of about 4 months]. PSA[01/18/2018]= 4.32 ng/mL



DCFpyL-avid foci in R side and posterior elements of T9 vertebra body



DCFpyL-avid focus in the right scapula



DCFpyL-avid focus in the inferior and anterior aspect of the left iliac bone

Case report

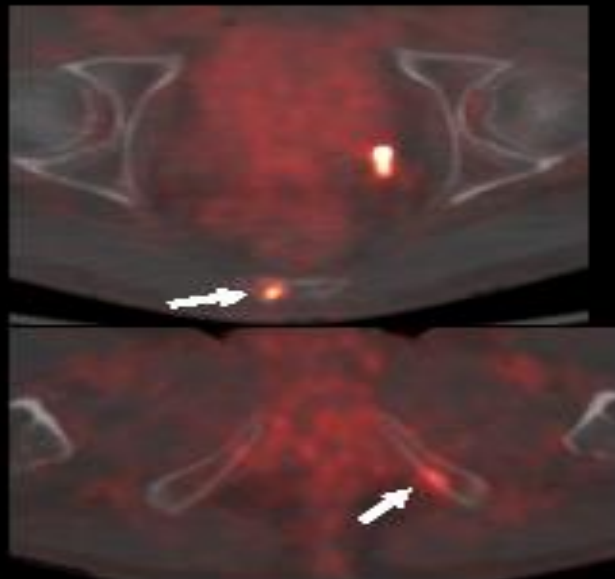
Protocol 17-C-089
DC FPyL #080_FU
7999063

Response to ADT

¹⁸F-DCFPyL PET/CT imaging

01/03/20

PSA: 13.59 ng/mL

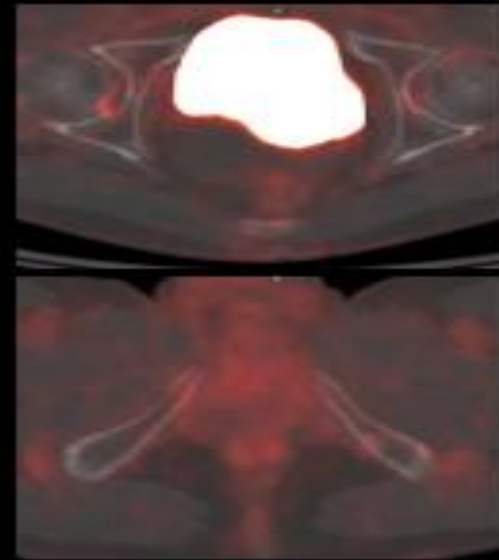


DCFPyL-avid sclerotic bone lesions
at the R lower sacrum and Left
ischium

¹⁸F-DCFPyL PET/CT imaging

10/05/20

PSA: 0.04 ng/mL

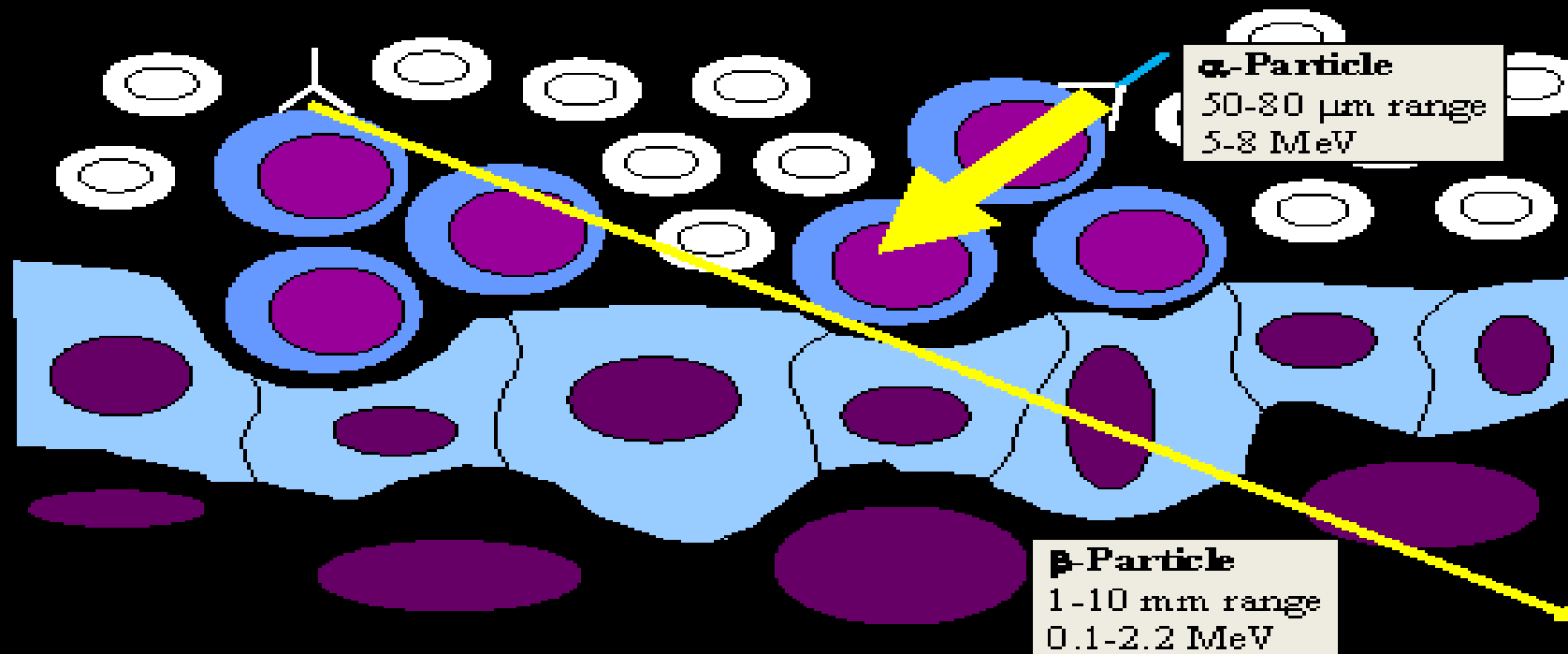


Interval complete resolution of the DCFPyL
uptake at the bone sclerotic lesions (R
lower sacrum and L ischium)- sclerotic
persists but the PSMA-PET uptake has
resolved.



Radionuclides

α - vs. β -Particle Radionuclide Therapy



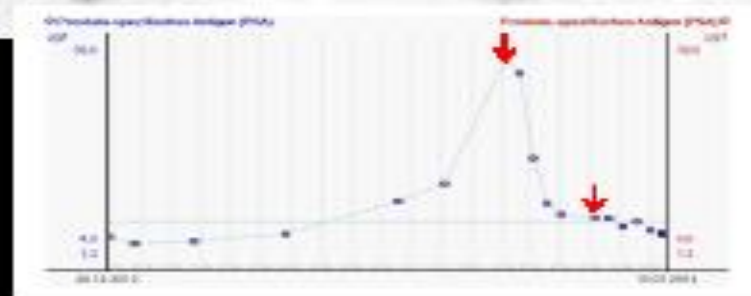
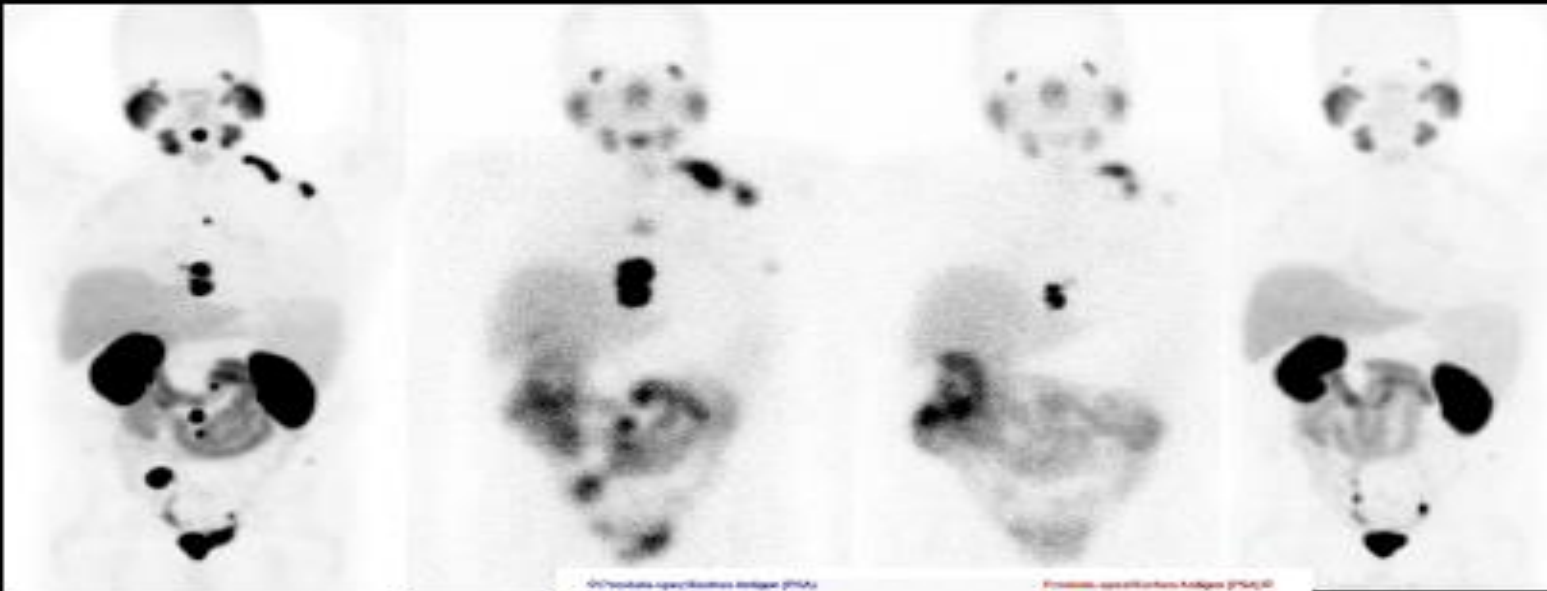
Case report

^{68}Ga -HBED-CC
03.12.13

3,3 GBq ^{177}Lu -
PSMA617 03.02.14

4,0 GBq ^{177}Lu -
PSMA617 5.05.14

^{68}Ga -HBED-CC
14.7.14



Freddie Giesel

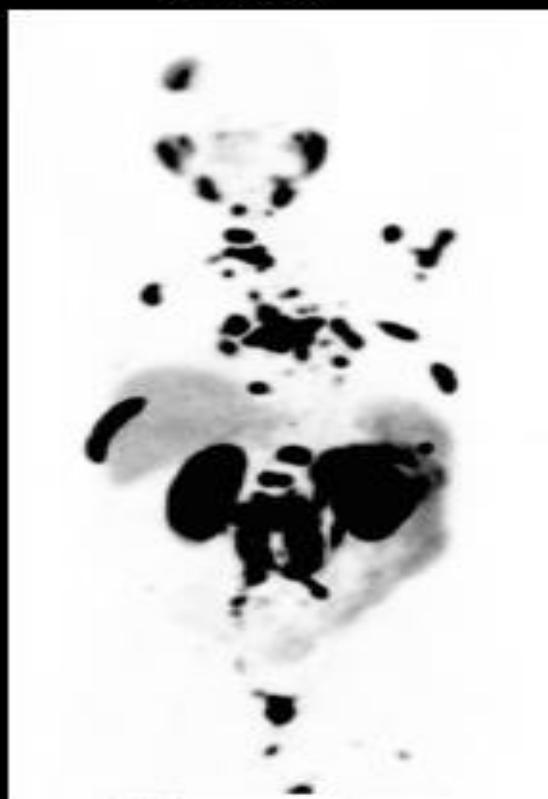
Frank Lin



^{177}Lu -PSMA617

Case report

4.2014



Prior to therapy

8.2014



2 x 8 MBq ^{225}Ac

12.2014

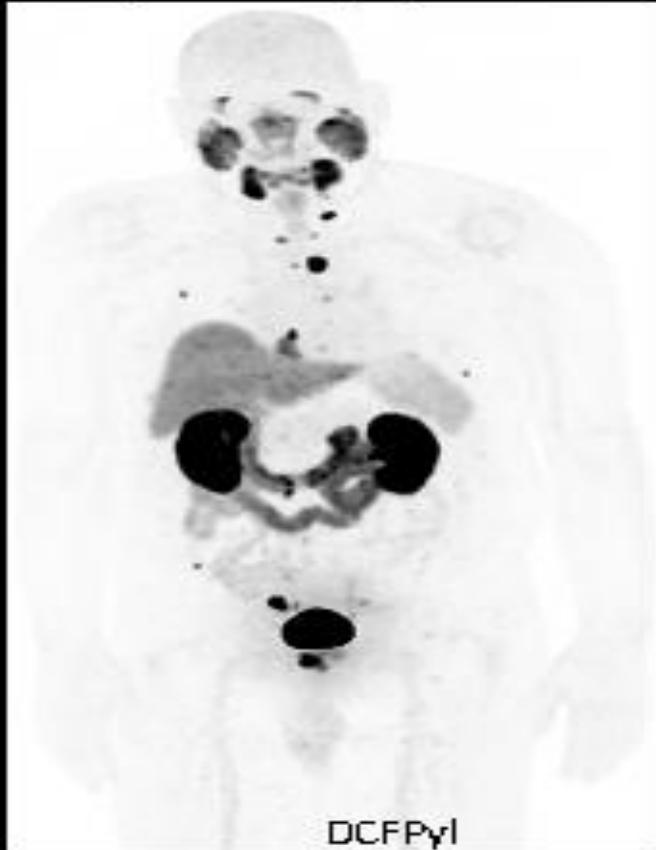


3 x 8 MBq ^{225}Ac

Case report

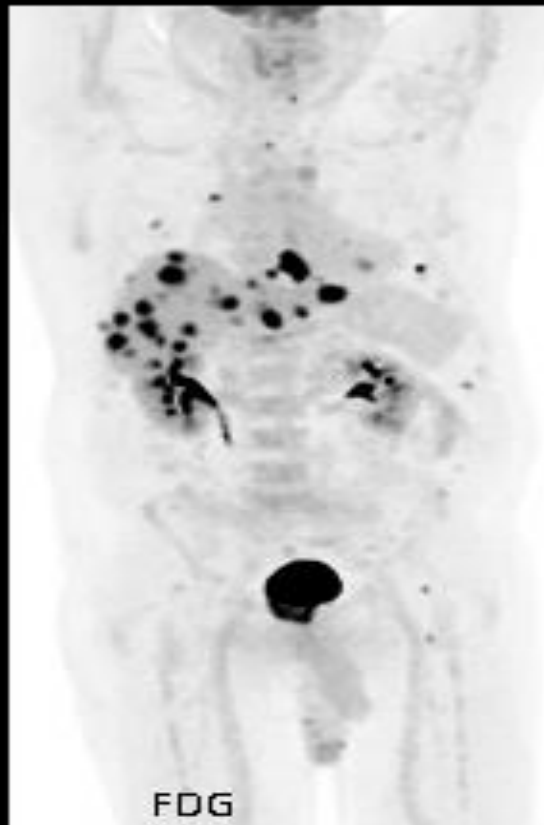
Protocol 17C-0089
DCFPyL # 00xx
Small cell variant

DCFPyL PET imaging



DCFPyL

FDG PET imaging



FDG

No significant abnormal DCFPyL uptake within the multiple FDG-avid liver lesions or within the FDG-avid bilateral pulmonary nodules

SUMMARY

PSMA PET/CT Summary

- PSMA PET imaging is a breakthrough technology for detecting recurrent and metastatic prostate cancer
 - Earlier and more precise therapy for recurrent disease
 - Better chance of cure
- PSMA can also be used for Targeted Radionuclide Therapy to kill cancers harboring PSMA+ cells
 - Efforts are ongoing to maximize treatment while minimizing side effects
 - PSMA “Window” may limit true extent of disease extent

SUMMARY

Overall Summary

- Diagnosis of prostate cancer is aided by use of MRI that can localize tumors for image guided biopsy (vs. random biopsy)
- MRI can be used to follow patients on active surveillance
- Once a patient undergoes therapy they can recur:
 - PSMA PET/CT is most sensitive modality for detecting recurrence
 - Disease can progress to metastatic disease
 - PSMA PET can be used to monitor patients although CT and bone scan are still the standard of care

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